AUDITORY DEVELOPMENT AND SENSITIVITY IN HUMANS MEASURED BY THE BRAINSTEM EVOKED RESPONSE (BSR)

By

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The dissertation is the final hurdle one must overcome in pursuit of the doctorate degree. As when all stressful, vigorous tasks are completed to the best of one's ability the individual is left with euphoria for obtaining one goal and optimistic anticipation in setting future ones. To achieve worthy research or academic goals the scientist/educator must have certain qualities: basic knowlege of the field, curiosity, imagination, enthusiasm, criticalness, and integrity. My special appreciation goes to the chairman of my supervisory committee, Dr. Donald C. Teas, for cultivating those qualities in his students and for the guidance and help he provided throughout my doctoral program.

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In recent years, the ability to accurately test the hearing sensitivity of infants and other difficult-to-test individuals has been advanced by the introduction of the auditory brainstem evoked response (BSR). The BSR is rapidly gaining in popularity among clinicians; however, there is a lack of adequate research on its limitations. In the present study, BSRs from normal infants, normal adults, and adults with hearing loss were examined in order to learn more about development of hearing in humans, the frequency specificity of the BSR, and its ability to measure hearing loss.

Stimuli were broad-band clicks (BB) and narrow-band filtered clicks (FC) at center frequencies of 1, 2, 4, and 8 kHz, presented monoaurally at 30/s. Latencies of waves I, III, V, and VA were chosen as the dependent variable for all subjects.

Latency *vs.* intensity functions (L-I) for each wave were obtained on: 10 normal adults, 6 adults with hearing loss,

and 50 infants between the ages of 4 to 48 weeks. The data from normal adults served as baseline for infants and subjects with hearing loss. On hearing loss subjects (selected for steep-sloping losses without notches in the audiogram) comparisons of behavioral pure tone (PT) and FC thresholds and BSR-determined thresholds were made and L-I functions were compared with normals.

Wave I could not be reliably recorded to the 1 kHz FC and it was occasionally recorded to 2 kHz FCs in normal adults and infants. The probability of detecting wave I improved for 4 and 8 kHz FCs and BB clicks. Waves III, V, and VA could be recorded to all stimulus conditions; however, the probability of detecting the responses increased with stimulus frequency and intensity. Data were collected on wave VA, the large-amplitude negative peak following wave V, to evaluate its usefulness as a supplement to wave V. Latency decreased with increase in stimulus frequency and intensity for all the waves. At 90 dB, all latencies, regardless of stimulus frequency, were equal to the 8 kHz value.

In subjects with hearing loss, BSR thresholds generally followed the pattern of the behavioral audiograms except BSRs were usually higher than PTs and always higher than FCs.

In infants, wave I showed no change in latency over age to BB clicks and 8 and 4 kHz FCs. An age effect (decreased latency with increase in age) may be present to the 2 kHz FC. No age effects were seen for any wave to 1 kHz 40 dB FCs while age effects were present on waves III, V, and VA at all

other stimulus conditions. The largest effects were to the 8 kHz stimuli.

Results from normal and hearing loss adult subjects suggested that frequency specificity of the BSR improves as intensity decreases; however, at 40 dB HL, a one-to-one relation between PT and BSR threshold does not yet exist. The wave I data from infants provide strong evidence that the cochlea in infants is fully functional in basal and second turn locations by 4 weeks of age. No direct data could be obtained from the apical turn. Development along the central auditory pathways appears to proceed in a caudal to rostral direction and in a low to high frequency tonotopic manner until sometime after one year of age. The use of the BSR in clinical determination of hearing loss was discussed and it was concluded that other tests should be used in addition to BSR. Both BSR threshold and L-I functions should be obtained in order to minimize errors in diagnosis of hearing loss.

CHAPTER I
INTRODUCTION

The human infant's capacity to respond to acoustic stimuli is of interest to developmental psychologists, sensory psychologists, otolaryngologists, and audiologists. The developmental psychologist is interested in auditory development because it is one element in the overall development of the human infant; the sensory psychologist is interested in the senses per se and the subtle mechanisms by which they function; the otolaryngologist is concerned about the abnormal infant, therefore knowledge of the normal one is necessary to quantify deviations and determine treatment; the audiologist must have the tools to accurately measure auditory function, find the degree of hearing deficit and plan appropriate habilitative action.

Each of these disciplines has developed procedures to assess auditory responsivity in the neonate and infant. The degrees of sophistication of these methods and procedures vary widely along with the information provided by each technique. In general, the procedures for measuring physiological changes in infants indicate lower thresholds than those techniques using behavioral observations as the response measure. Measures of infants' behavior are often less precise than for adults.

Over the years, the variety of physiological techniques available has generated a great amount of data on infant auditory responsivity. Some of these studies have attempted to define a threshold level for the infant response, while others use a moderately intense stimulus and are more interested in rates of response to different stimulus parameters. When dealing with infant auditory sensitivity or responsivity, the word "hearing" must be used with caution. A physiological response to an acoustic stimulus does not mean that the infant has "heard" the stimulus in the same sense that the adult can say, e.g., "Yes, I heard that." In the infant, the response is interpreted to mean that the neural pathways (specific to the measure used) are functional, and there is greater opportunity for the examiner to interpret the response. A review of some of the more common physiological measurement techniques used today and a summary of their findings are described below. Behavioral studies are not included because little quantitative data are available, and the more recent procedures are still under development.

Measurement Techniques

Heart Rate Response (HRR)

In the heart-rate procedure a criterion change in rate of about 3-5 beats/minute following an acoustic stimulus is accepted as indicating audibility. There are few studies that specifically search for threshold using the HRR, probably because of the time required to track the threshold.

Schulman and Wade (1970) found reliable HRR in infants greater than two months of age to narrow-band noise with center frequencies at 500 and 3000 Hz at 34 dB sound pressure level (SPL). Berg et al. (1977) obtained responses to 250, 1000, and 4000 Hz tones at 30-40 dB SPL in a group of 2-4 month olds. These studies suggested that acoustic stimuli were processed through quite complex neural pathways (peripheral hearing mechanism, brainstem, and heart rate regulatory centers) when presented at fairly low intensity levels in very young infants.

Studies using suprathreshold stimuli have shown that complex signals are more effective in eliciting a change in heart rate than pure tones. Effective stimuli are square waves and synthetic speech (Clarkson and Berg, 1978), tone chords (Turkewitz, Birch, and Cooper, 1972), and narrow-band noise (Schulman, 1973).

Respiration

Much of the work using change in respiration patterns as a measure of hearing sensitivity has been done by Bradford. Respiration is easily measured requiring only a strain gauge around the chest, the output of which is led to a pre-amplifier, and a strip-chart recorder. According to the procedure described by Bradford (1975) the acoustic stimulus is presented at the beginning of a respiration cycle and a response, indicated by a change in amplitude or pattern of the cycle, is considered valid only if it occurs during the next cycle. A third, post-response cycle is also observed. The first and third cycles serve as controls for

the middle cycle. The middle cycle must be different from the first and third in amplitude or waveform to score a response present. Although the results of the procedure are influenced by many factors (stage of sleep, activity level, and sedation), Bradford (1975) reported that thresholds to 1000 and 3000 Hz tones were obtainable at 0 dB Hearing Level (HL) in 24, 2 to 24 day old infants. These infants were re-tested by respiration measures at 4 months and again at one year with the same threshold results.

Cortical Evoked Response (CER)

By recording the cortical evoked response (V-potential, 90-150 ms latency) with signal averaging techniques, Engel and Young (1969) found that identifiable responses could be obtained from neonates at levels of 3-16 dB HL (International Standards Organization (ISO), 1964) over a frequency range of 150 to 8000 Hz. However, Taguchi et al. (1969) using frequencies of 500, 1000, and 2000 Hz, found thresholds (lowest intensity that a detectable response could be obtained) of 35-38 dB HL (ISO, 1964) for neonates up to 4 days when signals were presented by air conduction. When the signals were presented by bone conduction, they found an air/bone gap of about 11 dB prior to 2 days of age which disappeared by 4 days of age. After 4 days, thresholds by air conduction were about 28 dB across the frequency range used. This implies that the middle ear is not fully functional at birth. Barnett and Goodwin (1965) used click stimuli (75-2400 Hz) to elicit the CER on a group of 18 normal 2, 3, and 4 day old infants. They reported

that 11 out of 15 of the subjects had measurable CERs at a level of 35 dB. Intensity levels were described as dB relative to "adult waking threshold." In older (4-12 months) infants, Onishi and Davis (1969) reported 10-15 dB thresholds at 1000 Hz. They also reported that in infants the latency of the CER is longer than in adults.

The use of the CER as a valid and reliable measure of hearing threshold has recently been questioned. Rapin and Schimmel (1977) have discussed their experience using CER in a clinical setting. Using CER in a longitudinal (follow-up) approach, they tested children less than 2 years of age who were at risk for hearing loss and again a few years later by behavioral audiometry. The most common error made was to identify a CER as present when in fact there was no response (false positive). They concluded that CER should not be used as a clinical tool, but if it is, it should be only one of a battery of tests. In view of Rapin and Schimmel's findings, perhaps the above CER studies should be viewed as less than imperative, as indeed most critics do.

Electromyography (EMG)

Hutt et al. (1968) studied neonates 3-8 days old using EMG to record startle responses to acoustic stimuli. The signals were square and sine waves, of 2 seconds duration, at octaves starting at 125 Hz to 2 kHz, presented at 75 dB SPL. The results of their study, later re-analyzed by Weir (1976), showed that the highest probability of a response was to the complex (square wave) signal at 125 and 250 Hz,

with responses decreasing towards the higher frequencies. This was not a threshold study but does support other findings (particularly HRR) that complex, low-frequency sounds elicit more responses (Eisenberg, 1976). Higher responsivity to complex signals were confirmed by Lenard, Bernuth, and Hutt (1969) who used CER.

Auditory Brainstem Response (BSR)

The most recent tool used to study the human infant auditory system is the auditory brainstem response (BSR), first reported by Sohmer and Feinmesser (1970) and studied later by Jewett, Romano, and Williston (1970) and Jewett and Williston (1971). These reports described a series of 5 peaks of submicrovolt amplitude that appeared within 6 milliseconds (ms) poststimulus onset to a broad-band click presented at a moderate intensity. These responses can be recorded by surface, scalp electrodes. Subsequent studies (Lev and Sohmer, 1972; Buchwald and Huang, 1975; Starr and Hamilton, 1976) localized these peaks as originating at successively more rostral auditory brainstem centers. Roman numerals were assigned to the peaks in order of latency by Jewett and Williston (1971) and their suggested anatomical correlates are as follows: I - auditory nerve, II - cochlear nucleus (CN), III - superior olivary complex (SOC), IV - ventral nucleus of the lateral lemniscus (VLL) and V - inferior colliculus (IC). These short-latency, hence, low-order, responses were found to be unaffected by state of the subject, sleep, habituation, and drugs (Jewett and Williston, 1971;

Picton, Hillyard, Krausz, and Galambos, 1974). Other reported characteristics of the BSR are that wave V is the largest of the series (Jewett and Williston, 1971), and the latency of wave V increases as stimulus frequency decreases (Davis and Hirsh, 1976; Davis, 1976; Klein and Teas, 1978; Coats, Martin, and Kidder, 1979; Kramer and Teas, 1979). These characteristics of the BSR are drawing much interest in using these potentials for estimating auditory sensitivity in infants. The assignment of peaks to respective anatomical locations should be viewed with considerable caution. The neural activity represented by each peak probably represents combined activity from several nuclei or tracts rather than from a single generation.

Hecox and Galambos (1974) showed that for broad-band clicks (BB) presented at 60 dB HL the latency of wave V steadily decreased from birth and reached adult values at 1-1½ years. Hecox (1975) also looked at the age effects with BB clicks on waves I and III and found that wave III latency approximates the adult by 1-1½ years. Wave I could only be identified in 30% of the sample (15 out of 50) and the adult latency value was reached by 7 months. Since BB clicks can be expected to stimulate a wide range of cochlear locations, Hecox (1975) used selective high-pass masking to estimate the frequency-related contributions of the wave V response. He reported that the masker had little effect on the infant wave V until the lower cutoff was at 2 kHz. His interpretation of these data was that there is little contribution to

the wave V response from high-frequency fibers located in the base of the cochlea, which accounts for the increased latency. The latency decrease with age in the unmasked condition is then said to be due to a progressive addition of higher frequency contributions as the basal turn of the infant cochlea develops. However, the figure Hecox presented (Fig. 5.12, p. 183), plotting latency of wave V vs masker cutoff frequency with age as the parameter, does not entirely support this interpretation. In fact a sizable increase in latency (0.5 ms) occurs when the lower limit of the high-pass masker is decreased to 8 kHz (in a 10 day old). Unfortunately a similar study has not been performed using wave I. The average intensity found to elicit wave V (threshold) was 27 dB in the newborn compared to 10 dB in the adult.

Salamy, McKean, and Buda (1975) also used broad-band clicks presented at 60 dB HL, 15/sec, and found that wave V did not reach adult values until 2-1/2 years. In another study, Salamy and McKean (1976) measured the latencies of waves I, III, and V, then subtracted them to find the time required for neural transmission of the sensory volley from one responsive site to the next. Results showed that wave I latency for their click stimulus reached adult value by 6 weeks and that wave V required more than one year to reach adult values. Salamy and McKean suggested that the cochlea and cochlear nerve are fully functional by 6 weeks and the delayed latency of wave V, requiring central transmission, is due to factors such as myelination and synaptogenesis of the brainstem.

Effects of stimulus parameters

Rate. The rate at which stimuli are presented produce many conflicting results in the literature. In adults, Jewett and Williston (1971) and Klein and Teas (1978) found no consistent effect on the latency of wave V at rates up to 30/sec, while Don, Allen, and Starr (1977), Zollner, Karnahl, and Stange (1976), Terkildsen, Osterhammel, and Huis in't Veld (1975) found effects on latency in the same range of repetition rates. In infants, Hecox (1975) found no rate effects for clicks presented at 30 and 10/sec, while Salamy et al. (1978) found a significant rate effect on all the BSR waves regardless of age. The newborn had the largest wave V rate effect which was significantly different from the other age groups. Salamy's interpretation of rate effects is that the caudal brainstem is well myelinated shortly after birth, but the rostral brainstem (IC) may not be completely myelinated for as long as 3 years. Klein, Kramer, and Teas (1978) examined rate effects on wave V to FCs in infants. When stimuli were presented at 30 and 10/sec, wave V usually appeared to be longer in latency for the 30/sec rate to high-frequency filtered clicks, while little or no rate effect was seen for low-frequency filtered clicks.

Stimulus frequency. Many of the studies mentioned thus far used broad-band click stimuli to evoke the BSR. This stimulus is popular because it produces highly synchronous

nerve fiber discharges which result in clearly identifiable BSR peaks when the clicks are presented at moderate intensity levels. A shortcoming in using broad-band stimuli is that different regions along the cochlear partition cannot be selectively stimulated; thus, the effect of frequency cannot be measured. Tone bursts with long rise times are excellent frequency-specific stimuli; however they do not produce easily identifiable BSRs. Compromise stimuli, such as narrow-band (filtered) clicks (Davis, 1976; Zerlin and Naunton, 1975; Klein and Teas, 1978), short tone bursts with rise times of 1 to 2 ms (tone pips), or a single cycle of a sine wave (Gerken, 1978) have been used which produce an identifiable BSR that can be used to assess frequency effects. When such stimuli are presented at an appropriate intensity, latency of wave V is inversely related to stimulus frequency, apparently reflecting different sites of stimulation along the cochlear partition. These stimuli may provide the means for constructing an audiogram by BSRs.

Using filtered click stimuli Klein et al. (1978) reported that the latency of wave V in the 1-5 month old is equal to the adult for low-frequency filtered clicks, whereas wave V latency is longer than the adult to frequencies above 2 kHz. Responses could be recorded to high-frequency clicks at low intensity levels (10 dB) approximately equal to the adult threshold; however, this was not systematically studied.

Results from the infant BSR studies leave a confusing picture of the behavior of the BSR to different stimulus parameters and age effects. The observations described above suggest that the BSR can be recorded in infants at low intensity levels. This is in agreement with some findings for cortical responses, respiration measures, and observations on wave I, and suggests that normal cochlear function is obtained by 6 weeks of age. A factor that makes the above studies difficult to compare is the difference in acoustic stimuli used; Salamy (1975) used 50 μs clicks with Sennheiser Hd 414 earphones; Hecox (1975) used 100 μs clicks with Realistic earphones; Klein et al. (1978) used filtered clicks (FC) with TDH-39 earphones. Since FC stimuli are controlled for spectrum through calibrated earphones, frequency effects may be analyzed in the BSR, perhaps explaining some of the conflicting results across studies. For example, it was shown that the spectrum of the stimulus will influence the degree of wave V latency-change over age (Klein et al., 1978).

The anatomy of the infant auditory system is not fully documented. If the above physiological results are to have a valid or logical interpretation they must be consistent with the underlying histological and anatomical data. The following is a summary of the current data available on the development of the outer and middle ear, cochlea, and central auditory system (CAS) taken from animal and human material.

Developmental Anatomy and Physiology

Outer and Middle Ear

The outer ear is fully developed by birth; however, its size does not reach full dimensions until sometime after 1 year of age (Kirikae, 1960, referenced in Hecox, 1975). Middle ear ossicles are nearly adult in size by the 25th fetal week and are histologically mature in the newborn (Anson, 1973). Pneumatization of the middle ear cavity (epitympanum and tympanum) is complete by the 9th fetal month and formation of the antrum and mastoid air cells beginslate in fetal life and continues into childhood (Anson, 1973).

The electroacoustic impedance bridge, a device used primarily by audiologists to measure middle ear compliance, has been used to measure the compliance of the neonate's tympanic membrane (TM). Keith (1973, 1975) measured the static compliance and compliance change versus pressure change (tympanometry) in neonates 2.5 to 151 hours old and generally found compliance values corresponding to a high-normal range in the adult. Keith concluded that middle-ear mobility in the neonate is essentially normal, contradicting the long standing notion that the middle ear cavity is filled with mucus or embryonic mesenchymal tissue until a few days after birth. This conclusion may be questionable in view of the recent findings of Paradise, Smith, and Bluestone (1976). They performed impedance measurements and otoscopic examinations and compared these results to findings when

myringotomy was performed. For infants less than 7 months, they found that abnormal (flat) tympanograms were correlated with middle-ear disorders; however, normal tympanograms were not of diagnostic value, i.e., a normal tympanogram could be obtained in the presence of middle-ear effusion. They attributed this finding to the fact that the ear canal of the infant is highly compliant; therefore it may be the compliance of the ear canal that is being measured in the presence of stiff TM. One way to differentiate whether the TM or the ear canal is contributing to a normal tympanogram is to use the stapedial reflex. If the compliance of the canal is being measured, then a reflex should not be obtained indicating the TM is immobile. If the TM is of normal compliance, it should be reflected by the presence of a reflex, assuming that the inner ear is normal. However, the stapedius reflex is difficult to elicit in the normal neonate and may not provide a practical solution (Walker et al., 1977).

Taguchi et al. (1969) obtained cortical evoked response measurements in newborns to acoustic stimuli presented via air and bone conduction. They found a 15 dB air/bone gap within 2 days of birth which disappeared by 4-5 days. This study did suggest that there is a middle-ear occlusion or an alteration of the outer- and middle-ear transfer function present at birth.

Whatever the status of the newborn middle-ear may be, all evidence suggests that by a few weeks of age the middle ear is mature and functionally normal. Since the size of

the external ear canal is changing with age, it is possible that the resonances of these structures are also changing, which would result in variations in the transfer function, i.e., to produce an apparent change in sensitivity of inner ear responses that would actually reflect alterations in the effects of acoustic pressure at the stapes.

Inner Ear

The most in-depth study of the maturational pattern in the human cochlea was reported by Bredberg (1968). He found (1) that differentiation in the fetal cochlear begins near the basal end and progresses towards apex and base; (2) the differentiation of the inner hair cells (IHC) precedes that of the outer hair cells (OHC); (3) the newborn infant had the most completely intact population of hair cells of the entire sample studied ranging from fetus to adult. Thus, on a gross histological level the hair cell population appears to be completely present at birth. The tunnel of Corti is present in all turns by the 21st fetal week and the otic capsule attains the adult size by the 25th fetal week (Anson, 1973). On a more subtle level there may be incomplete development, such as at the hair-cell, nerve-fiber synapse, which can only be observed under the electron microscope (EM) - a study not yet performed in the human.

Electron microscopical studies of this nature have been performed on animal preparations, however. Pujol, Carlier, and Devigne (1978) examined the development of the kitten cochlea by EM. They reported that the IHCs reached maturity

before the OHCs, but the most intriguing finding was the plasticity of the innervation pattern. At birth the efferents are reported to synapse directly on the IHC; however, by one week, the number of efferents decrease and the afferents increase to seemingly "push away" the efferents. On the OHCs, afferent fibers appear before the efferents; thus, in the kitten, there appears to be much microanatomical neural development occurring within the cochlear system. The immaturity of sensory structures in the kitten is grossly evident, even from casual observation, and appears to contrast rather strongly with the human infant. One cannot, of course, superimpose the developmental sequence determined for the cat upon the human; however, the animal data can suggest possible interpretations for structural changes underlying alterations in functional measures in the human. Perhaps the infant cochlea is not fully functional at birth because hair cell-nerve fiber relations are not completed.

Pujol and Abonnenc (1977) studied the development of the golden hamster cochlea by light microscopy (LM) and EM. LM findings showed that the cochlea was very immature at birth and attained the look of a completely mature cochlea after 25 days. The maturational sequence of hair cell development and other cochlear structures was in a basal-to-apical direction. The EM findings revealed that synaptic development was more advanced on IHCs and afferents matured before efferents. The animal data are consistent with the

observations of Bredberg - on the human - that the mammalian cochlear maturational sequence is predominantly in a basal-to-apical direction.

Central Auditory System (CAS)

The CAS is composed of a series of nuclei with ipsi and contralateral innervation which provide the means for binaural interactions and extensive neuronal processing. From the most caudal to rostral extent, these nuclei are: cochlear nucleus (CN); superior olivary complex (SOC); the large contralateral pathway, the trapezoid body (TB) and its major nucleus, the medial nucleus of the TB (MNTB); the ventral and dorsal nuclei of the lateral lemniscal system (VLL, DLL); the inferior colliculus (IC); the medial geniculate body (MGB), and finally, cortex. There is also a descending system that parallels the ascending systems. Little anatomical developmental data exist on these pathways in human or animal material. Other than the infant BSR findings, there are no human developmental physiological data, but some animal data are available.

Myelination of the human infant brainstem was studied by Rorke and Riggs (1969) who reported that, at term, the TB, SOC, DLL and VLL are myelinated, but the IC contains very few myelinated fibers. Another study by Yakovlev and Lecours (1967) reported that the VIII nerve is myelinated by the 5th fetal month and myelination of the TB, LL, and IC begins in that same month. By the 9th fetal month the myelination cycle is complete. It was not quite clear if

the authors included the IC in the completed cycle. If so, this conflicts with the Rorke and Riggs report. Rorke and Riggs noted that gross inspection of tissue stained for myelin may be misleading because both cells and background substance will stain during the period of myelin development. Tissue must be under microscopic study to determine if the cells are myelinated.

The cytological development of the CN in the cat has been observed extensively in a series of studies by Cohen (1972) and Kane (1973). Under light microscopy the octopus cells in the posteroventral CN appeared mature by 10 days postnatal (Cohen, 1972; Kane, 1973). However, under electron microscopic (EM) study, these cells did not mature until after 3 weeks postnatal (Schwartz and Kane, 1977).

The latency of the gross potential recorded from the cat CN by Pujol (1972) decreased with age reaching the adult value by 17 days; unfortunately, the acoustic stimulus used was not specified. Romand and Marty (1975) reported that units in the dorsal CN (DCN) and ventral CN (VCN) of the cat reached adult latency by 1 month postnatal; however, the average discharge rate did not. Saunders, Coles, and Gates (1973) studied the development of the chick CN with gross potentials and showed that only responses to low and mid frequencies at high threshold levels could be obtained in the youngest chicks. As age increased, thresholds decreased, and the range of responses increased toward high frequencies.

The anatomical development of the SOC was studied by Strominger and Hurwitz (1975) using human infant material. They reported that cells in the infant medial superior olive (MSO) are more "plump," more densely aggregated, and contain more cells in a given section than in the adult. The infant lateral superior olive (LSO) also contained more cells than the adult, and the entire SOC was more condensed.

Physiological development of the IC was studied by Aitkin and Moore (1975) by means of unit recordings from the IC in kittens. They reported that units with low characteristic frequencies (CF) were predominant at the youngest age, and these had broad tuning and high thresholds. As age increased, high-CF units began to appear, tuning became sharper, and thresholds for all units decreased. Pujol (1972) reported that gross potentials from the IC in kittens showed latencies that decreased with age, matching adult values at 25 weeks.

The preceding summary suggests that much development is taking place in the CAS in humans and animals for some time after birth. The trend is that primarily low-frequency stimuli elicit responses at the earliest ages, with high-frequency responses appearing later. The maturational sequence of the CAS appears to be in a caudal to rostral direction. The infant BSR (wave V) studies are consistent with this finding.

Present Study

The purposes of the present study are, primarily, to examine frequency effects on the latencies of response peaks in the infant BSR, and secondarily, to study frequency specificity of the BSR. It has been firmly established that the more basal portions of the cochlear partition will contribute most heavily to the whole-nerve response when a wide-band stimulus is used (Teas, Eldredge, and Davis, 1962). Thus those BSR studies (Hecox and Galambos, 1974; Hecox, 1975; Salamy et al., 1975; Salamy and McKean, 1976; Salamy et al., 1978) employing only broad-band clicks are limited in their investigative range. They cannot examine the maturational sequence at more apical regions along the cochlear partition as reflected by the latency change of wave I. Filtered clicks will allow somewhat selective stimulation of different cochlear locations and associated pathways in the CAS. Thus the infant BSR may be dissected into frequency specific components and the behavior of each component over age may be individually analyzed. To establish baseline data, normal-hearing adults are used.

There are a variety of techniques available to study frequency specificity of the auditory evoked potential. The use of selective masking was first introduced by Teas et al. (1962) when studying the whole-nerve response in guinea pigs. This technique was adapted for work on the human VIII nerve response (Elberling, 1974), and the BSR (Parker and Thornton, 1978, a, b; Kramer and Teas, 1979).

By changing band-width of the noise masker, contributions from selective areas along the cochlear partition may be eliminated from the gross potential leaving the response produced in the unmasked regions. Another method of eliminating regions along the cochlear partition to study responses from remaining regions is by the use of subjects with hearing loss. By using adults with hearing deficits, frequency specificity of FCs and the validity of BSR - determined thresholds may be directly evaluated. This technique will be used in the present study. The frequency region where the hearing deficit exists should not contribute to the BSR; therefore, any responses obtained may be localized to frequency regions in which little or no deficit exists. Using subjects with hearing loss rather than using normals and simulating hearing loss with a masker enables evaluation of another parameter of the BSR: ability of the BSR to determine thresholds in clinical usage.

CHAPTER II
METHODS

Subjects

Normal Adults

Ten normal hearing students with thresholds 10 dB (ANSI, 1969) or better at octaves beginning at .25 to 8 kHz with no history of ear disease were chosen. All were female between the ages of 20-26 years.

Hearing Loss Adults

A group of adults with hearing losses was obtained through the University of Florida Speech and Hearing Clinic. History of the hearing loss was gathered from the clinic records and by interview by the experimenter (E). Only those patients with hearing loss that appeared to be the result of an irreversible cochlear problem, i.e., presumed hair cell loss secondary to noise exposure, prebycusis, etc. were selected as subjects. Etiology of the hearing loss was estimated by history and audiometric test results. A total of 12 patients served as subjects. Nine were males and three were females with ages from 20 to 65 years.

Infants

Letters were sent to parents of newborn infants whose names were obtained from the birth records at the Frank M. Hall Health Center located in Gainesville, Florida. Only

infants determined normal by the obstetrician were queried. Because of the time required to contact the parents and scheduling the infant, the earliest age that testing began was at 3-4 weeks.

Equipment

Stimuli

The acoustic stimuli, filtered clicks (FC), were generated by ringing two bandpass filters (Krone-Hite, 330 MR and 330 M, 24 dB/octave each) wired in series, with a square wave pulse. High and low-frequency cutoffs were set to the same value and the duration of the pulse was adjusted to produce the desired waveform (Davis and Hirsh, 1976; Klein and Teas, 1978). The output of the filter was amplified (JBL SE 400S), attenuated (Hewlett-Packard, 350 D) and led to an oscilloscope (Tektronix, RM 561A) and rotary switch. The switch allowed the E to turn the signal on or off to the subject's earphone (TDH-39 in MX41AR cushion). The subject was in a double-walled, shielded, sound-treated room (IAC).

The center frequencies of 1, 2, 4, and 8 kHz and a 0.1 ms broad-band (BB) condensation click were used. The spectrum of the earphone output was found by measuring the acoustic output in a 6-cc coupler (Type 9A) and sound-level meter (Bruel+Kjaer 2203). The output of the meter was fed to a wave analyser (General Radio 1900A) using a bandwidth of 10 Hz except for the 8 kHz FC where 50 Hz was used. The records, obtained in linear form, were redrawn on logarithmic scales for clarity and are shown in Fig 1. The meter outputs showing the time waveforms were drawn in Fig 2.

Fig. 1. Amplitude-density spectra for FCs. The frequency of maximum energy is equal to the filter settings except at 8 kHz where the filter settings were at 9 kHz. See text for details.

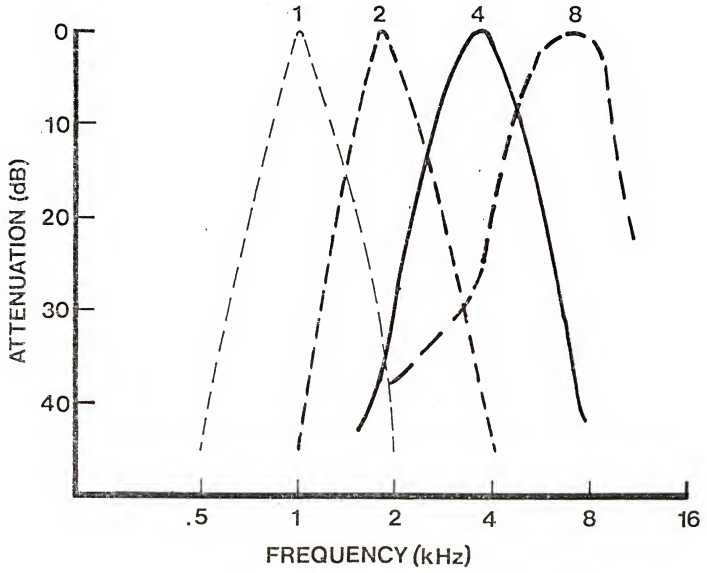
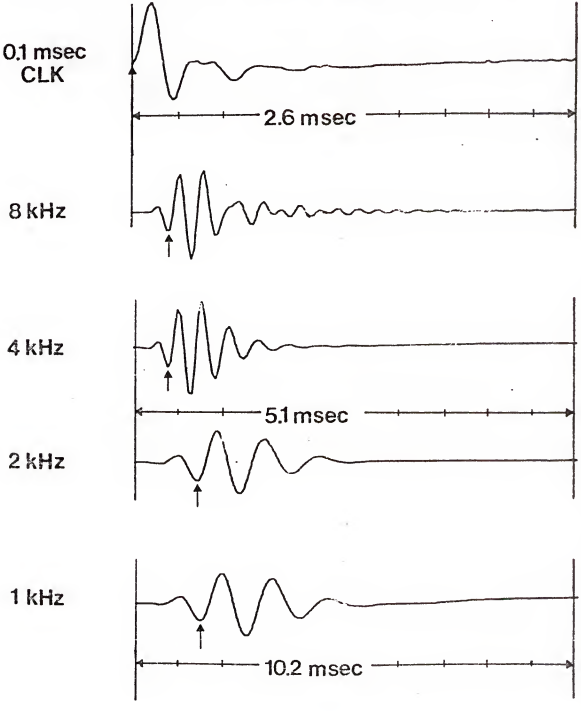

1
2
4
8
0
10
20
30
40
ATTENUATION (dB)
.5
1
2
4
8
16
FREQUENCY (kHz)

Fig. 2. Time waveforms of BB click and FCs. Each FC waveform is similar containing 4-5 cycles but duration and rise-fall time increases as frequency decreases. Arrows indicate the point from where BSR latencies were measured. Markers on the time scales represent 0.1 of the total time span.

ACOUSTIC OUTPUTS
(TDH–39)



Intensity levels were established by obtaining averaged thresholds by method of limits to FCs presented at a rate of 5/sec, from 5 normal-hearing adults (Klein, 1976; Klein and Teas, 1978). The clicks were presented continuously and the S was instructed to raise his hand as long as he could hear the clicks and lower his hand when he could not. The E adjusted the intensity in 1 dB steps until the S was uncertain that he could hear the continuous click train, i.e., his hand would go up and down without changing the stimulus level. This point was called threshold. This threshold voltage level was established as 0 dB hearing level (HL). The corresponding peak equivalent (p.e.) SPL was obtained by introducing a continuous tone of the same frequency as the FC and equal in peak-to-peak voltage into the earphone. The earphone outputs were measured with a 6-cc coupler as described above. The p.e. SPL of the FC was referenced to the SPL of the tone. The energy levels for FCs in dB SPL were computed by delivering the FCs at a rate of 50/s into a true rms voltmeter (Ballatine 321) calibrated so that the SPLs were read from rms voltage levels. The total energy for 5 clicks/s was calculated for each filter setting and the corresponding p.e. SPLs are listed in Table I. This procedure is similar to the method described by Yost and Klein (1979). All intensity levels used in this report are in dB relative to the behavioral thresholds as described above.

Table I. Intensities for FC thresholds corresponding to 0 dB HL determined on 5 normal hearing subjects. Levels are expressed as total energy (dB SPL) in five clicks over 1 S, and the corresponding p.e. SPL. Measurement procedure is described in text. The 3.0 dB value at 8 kHz may be underestimated because of compensation for the earphone rolloff at 8 kHz.

Frequency (kHz)	Energy (dB SPL)	p.e. SPL
8	3.0	32.3
4	1.0	25.8
2	4.0	23.6
1	4.5	23.6

Data Acquisition

The EEG was recorded with silver/silver chloride disk, (9 mm) surface, electrodes. Three electrodes were used, one placed on the forehead immediately below the hairline, and one on each mastoid. After skin was cleaned with alcohol and slightly abraded with electrode paste (Redux), the electrodes were coated with paste (Grass, EC2) and taped to the prepared locations. Resistance between electrodes was checked, and if it exceeded 5 k ohms the electrode was removed and the cleaning process repeated. This generally improved the resistance to within the 5 k ohm tolerance. However, on a few adults and infants, electrode resistance remained high (5-10 k ohms) even after repeating the application procedure three times.

The electrode leads were connected to a high-impedance (2×10^{11} ohms) cathode follower (Grass, HIP 511B) which led to an ac-coupled, high-gain amplifier (Grass, P511). The forehead lead was connected to the active (G1) terminal, the lead from the mastoid on the ipsilateral (stimulated) ear to the reference terminal (G2), and the other mastoid lead to ground. With this configuration, positive neuroelectric activity at forehead relative to mastoid appeared as an upward peak. Gain was set at 100 K and bandpass from 0.03-3 kHz.

In the early stages of this experiment the infant data were stored on FM tape (Ampex, FR-100A) with a bandpass from 0-2500 Hz at 7-1/2 ips, for later off-line averaging and analysis. Comparisons of the on-line averaged response

waveform and the same data averaged off tape showed an increase in response latency of 240 μsec for the taped data. The computer was programmed so that a delay of 240 μsec was introduced in the off-line average in order to compensate for this discrepancy. Immediately before averaging (on-line or off-line), the data were further filtered (Krone-Hite, 330MR) at 70-1600 Hz. Signal averaging was performed by a general purpose computer (DEC PDP 8/e). A dwell time of 79 μsec and 256 points were used which gave a total sampling sweep of 20.2 msec. The software included artifact rejection which was set to eliminate voltages greater than $\pm$ 7.0 μv from the average. A cursor was available which could be set to read the latency and amplitude values of desired waveform peaks of the completed average directly from the display scope. A hard copy of the waveform was obtained with an X-Y plotter (Houston Omnigraphic, 2000). About midway through the acquisition of the infant data and before the adult data gathering began, the software was modified so that the averaged waveform along with subject information could be stored directly on floppy disk (Data Systems, DSD 210-8). Once this system became operational, the FM tape was no longer used. All previously recorded data were re-averaged and stored on disk files.

Procedure

Acoustic stimuli were presented to all Ss monaurally to the ear ipsilateral to the mastoid reference electrode at a repetition rate of 30/sec. When the presence of a BSR was questionable, or a peak was ambiguous, the run was repeated

and if the waveform was similar in shape or the latencies of the peak in question were within ± 0.2 ms, the response peak was considered present. After the electrodes were attached, the S was allowed to lie down on a small bed in the sound-treated room. Subjects were strongly encouraged to sleep and many did, but if they could not, they were instructed to remain as still as possible during an averaging run. Waveforms were accepted for analysis if the number of computer-determined rejected samples were 10% or less than the total number of responses in the averaged waveform. If the number of rejected samples were greater than 10%, the EEG was considered to be too noisy and the S was again requested to relax.

Normal Adults

All stimulus conditions were not always completed in one session for every subject so return visits were required. The complete series, presented at 30/sec, consisted of: broad-band click (100 μs) (BB), 60 dB; 1 kHz FC, 40 and 60 dB; 2 kHz FC, 40, 60, 70, 80 and 90 dB; 4 kHz FC, 40, 60, 70, 80, and 90 dB; and 8 kHz FC, 40, 60, and 70 dB. The number of responses/ waveform ranged from 1000 for a high level, high frequency stimulus to 4000 for a low level, low frequency stimulus. The latency of waves I, III, V, and VA were found with the cursor readout which gave values in .079 ms steps.

Hearing Loss Adults

Instructions for adults with hearing losses were the same as for normal adults. Before the BSR recordings began, behavioral thresholds to FCs were established by method of limits. Once the thresholds were obtained, the S was given time to relax, and when the EEG voltage (RMS) was down to an appropriate level, the session began.

Filtered clicks were presented at suprathreshold levels beginning at 10 dB sensation level (SL) and increased in 10 dB steps until a BSR was noted. Latencies and amplitudes of all BSR waves were noted. If a BSR was obtained on the first presentation, the signal intensity was decreased 10 dB. The BSR threshold was considered to be the lowest intensity level (10 dB steps) at which an averaged response was observable. A control run with no signal present was included to have a record of averaged baseline activity.

Infants

Infants were scheduled as near to their usual nap time as possible. The mother was instructed to keep the infant awake before the experiment as best she could. If the infant was scheduled for the afternoon, it was requested that he not be given a morning nap at all, or a very short one. While mother held the infant, the electrodes were attached. Once the electrodes were in place, the E left the sound-treated room and the mother would try to induce sleep in the infant, either by holding him, or placing him in a crib. If the infant slept while the mother held him, she was

given the task of holding the earphone gently in place against his ear. If the infant was in the crib, the earphone was placed over the upturned ear, held in place by the force of its own weight. The mother remained in the test room throughout the experiment and was instructed to let the E know immediately, via an intercom, if the earphone was removed. All infant data were collected while under sleep -- no drugs were used. The average sleeping time per infant was about 45-60 minutes.

The entire protocol required about one hour to complete. Stimuli were presented in the following order: BB click, 60 dB; 1 kHz FC, 60 and 40 dB; 8 kHz FC, 60 and 40 dB; 2 kHz FC, 60 and 40 dB; 4 kHz FC, 60 and 40 dB (70, 80, and 90 dB were used on 5 Ss).

At the completion of the test protocol, or when the infant awoke and the BSR recording was terminated, middle ear impedance (tympanometry) was performed (Madsen, ZS76). Compliance values were taken and recorded at 200, 100, 0, -100 and -200 mmH_2O. If impedance results showed an abnormal tympanogram, a middle-ear disorder was suspected and the data for that session were not used.

The return visits were spaced at 4 week intervals for the first 4 sessions, and then at 8 week intervals. However, this schedule could not be followed closely because of cancellations due to sickness, vacations, and equipment breakdowns. An attempt was made to test the same ear on

return visits but this was not always possible because some infants insisted upon sleeping in different positions at different sessions. Parents were compensated for their time at $2.50/hour increasing $.50/hour every other session.

Data Analysis

Normal Adults

Latencies of waves I, III, V, and VA for each S were measured with the cursor readout. Mean latencies were computed and used to construct latency by intensity (L-I) functions for each wave for each FC. The mean latencies served as reference or target latencies for infants and the L-I functions were used for comparison with subjects who showed hearing losses.

Hearing Loss Adults

Behavioral pure tone (PT) and FC thresholds, and BSR thresholds for each S were compared for intrasubject consistency and with the normal adult values. When possible, L-I functions were obtained and compared with L-I functions for normal adults. A correction factor (CF) for frequency specificity of FCs was determined by relating the behavioral (PT and FC) to the BSR thresholds and was applied to normal, adult and infant subjects. The CF will be described more fully in the discussion section. The use of the BSR for hearing threshold estimation was examined.

Infants

Latencies of waves I, III, V, and VA were measured as for the adults. The latencies for each FC at each intensity

for each infant was plotted and the regression equations $Y = m \log X + b$ where Y = predicted latency, m = slope, b = Y intercept, and X = age, were computed for age *vs* latency for each wave. Mean normal-adult latencies served as targets for the regression lines drawn from the regression equations. Latencies from those infants tested longitudinally were compared to the regression lines previously determined from the whole infant sample. A more exact estimate of frequency regions (represented in the cochlea) actually stimulated by FCs was given by results from subjects with hearing loss.

CHAPTER III
RESULTS

Normal Adults

Some Ss had a great deal of difficulty relaxing and little data were collected due to the large number of artifact rejections. These subjects were not asked to return to complete the series. Therefore, some Ss do not have data at all stimulus conditions.

Waveforms

An example of a normal adult's BSR waveforms to a 4 kHz FC at different intensities is shown in Fig. 3. Response waves are labeled according to the Jewett convention except wave VA which will be discussed later. As previously reported (Klein and Teas, 1978; Davis, 1976) the amplitude of wave V decreases and latency increases as stimulus intensity decreases. This occurs for all FCs used. Amplitudes of the earlier waves decrease faster than wave V, particularly at signal levels below 80 dB. At 40 dB, waves I and III are often slightly above noise level. For this reason, the identification of waves I and III at low intensity levels becomes difficult, and at times impossible. If response waveforms showed multiple peaks in this latency region, the largest peak was chosen, or if there was no clear major peak, the midpoint of the top of the wave was the point at which latency

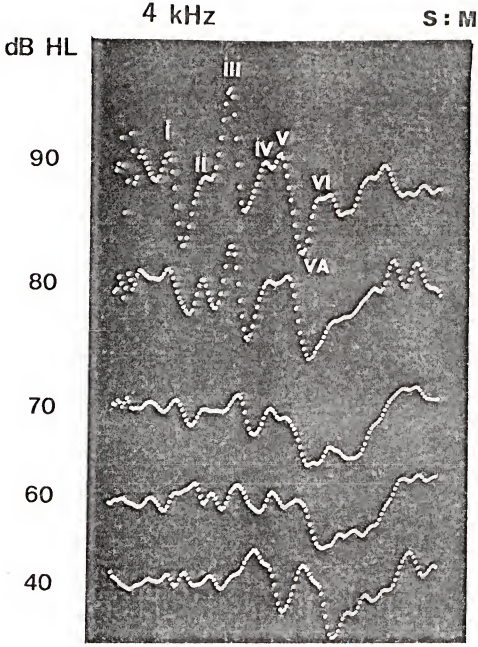
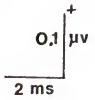


Fig. 3. Brainstem response waveforms from an adult with normal hearing. The stimulus was a 4 kHz FC presented at the above levels. As intensity decreases, waves become ambiguous, particularly wave I. Note the change in the IV-V complex as intensity is decreased. Forehead positivity is shown in the upward direction in this and all future figures.



was measured. Although larger in amplitude, wave V can become ambiguous at low intensity levels. At 80 and 90 dB wave V is slightly greater in amplitude than wave IV, but at lower intensity levels, wave IV may become larger (Fig. 3). At 40 dB it becomes uncertain whether wave IV is absent, is the highest peak, or if wave V is the highest peak or the shelf following the peak. This ambiguity is characteristic of BSRs from many normal Ss. The criterion for wave V identification in this study (the most positive peak preceding the change to negativity) requires that only the highest peak be labeled wave V. To label the shelf as wave V (Rowe, 1978; Chiappa, Gladstone, and Young, 1979) was considered, but many times the shelf following the peak was completely absent or only slightly visible. In order to be consistent in the wave V latency measurement the highest peak was always chosen. If subsequent research should show that this peak is better considered as wave IV, then the wave V latency measurements reported here for low intensity levels may be underestimates.

Probability and Variability of BSR Peaks

The means and standard deviations (SD) of latencies about the respective means of waves I, III, V, and VA were computed. Since the number of opportunities for obtaining a response was known, the number of responses actually obtained allowed the relative frequency, or probability of response (POR), to be calculated. These statistics are shown in Table II. As stimulus frequency and intensity decrease, the POR decreases and the SD increases. This finding is consistent with a

TABLE II. Probability of response (POR) and standard deviation (SD).

FREQ.	INTEN.(dB)	I	III	V	VA
BB	60	0.73(0.287)	0.73(0.242)	1.00(0.288)	1.00(0.348)
8 kHz	70	0.80(0.137)	1.00(0.125)	1.00(0.254)	1.00(0.270)
	60	0.67(0.153)	0.89(0.118)	0.95(0.236)*	1.00(0.270)
	40	1.00(0.211)	1.00(0.187)	0.94(0.264)*	1.00(0.283)
4 kHz	90	0.86(0.116)	1.00(0.106)	1.00(0.266)	1.00(0.197)
	80	1.00(0.142)	1.00(0.157)	1.00(0.236)	1.00(0.211)
	70	1.00(0.157)	1.00(0.152)	0.88(0.204)	1.00(0.249)
	60	0.67(0.348)	0.78(0.169)	1.00(0.275)*	0.78(0.449)
	40	0.50(0.551)	1.00(0.309)	0.89(0.310)*	0.89(0.370)
2 kHz	90	0.33(-----)	1.00(0.136)	1.00(0.196)	1.00(0.298)
	80	0.71(0.173)	1.00(0.241)	0.86(0.212)	1.00(0.397)
	70	0.75(0.156)	1.00(0.163)	1.00(0.233)	0.75(0.352)
	60	0.40(0.046)	1.00(0.259)	0.95(0.276)*	0.90(0.563)
	40	0.11(-----)	0.67(0.571)	0.90(0.380)*	0.80(0.532)
1 kHz	60	----------	0.73(0.524)	0.95(0.473)*	0.73(0.481)
	40	----------	0.70(1.048)	0.80(0.862)*	0.78(1.270)

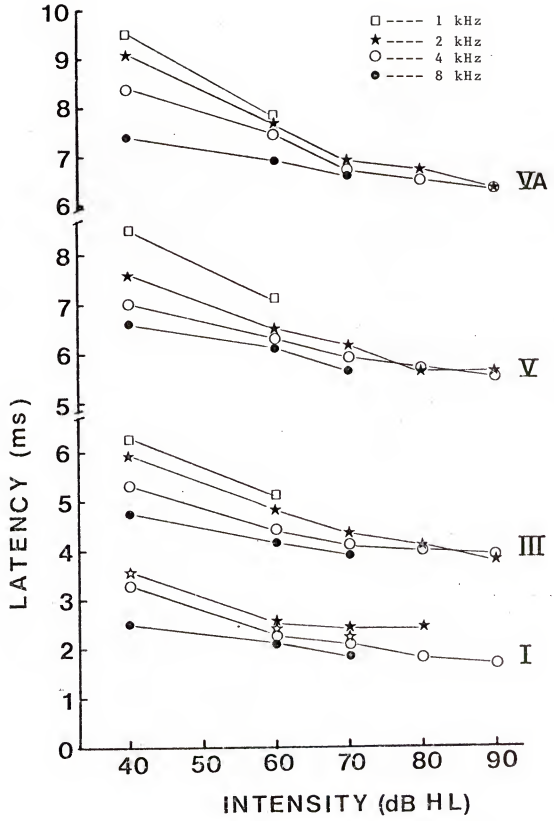
First number is % of responses present; number in ( ) is SD.
* = data from Klein and Teas (1978) pooled with present data.

decreasing signal-to-noise (S/N) ratio of the responses as stimulus intensity decreases, making the response undetectable, or ambiguous with multiple peaks (see Fig. 3, 40 dB). Decreasing frequency has a greater effect on decreasing the POR and increasing the SD than decreasing intensity. No clear wave I could be observed for 1 kHz FC at 40 or 60 dB, and for 2 kHz, wave I was observed in 40% of the opportunities at 60 dB and only 11% at 40 dB. The mean latencies for those cells that contain a low POR and a large SD are less secure estimates than cells with a high POR and small SD. For example, the mean latency of wave I at 4 kHz 40 dB is probably a less secure estimate of the true population mean than that at 4 kHz, 60 dB.

Latencies as a Function of Frequency and Intensity

The cursor readout provided latency values in 79 µs steps. Figure 4 shows the mean latencies as a function of intensity for waves I, III, V, and VA. The parameter is center-frequency of the FC. Wave I to the 2 kHz, 40 dB FC had a POR of only .11 (Table II) and was not considered valid; therefore, the data point was taken from Kramer and Teas (1979) (open stars) who used an ear canal electrode which provides a larger S/N ratio. They presented their stimuli at a rate of 10/sec and alternated polarity of the signal to cancel artifact and cochlear microphonic (CM). Data points from Kramer and Teas (1979) for 60 and 70 dB were also plotted for comparison with the wave I data from the present study. Good agreement exists for the 60 dB point and about a 0.2 ms

Fig. 4. Mean normal-adult latencies of BSR waves plotted as a function of intensity. The parameter is FC frequency. At 8 kHz, maximum intensity available due to equipment limitations was 70 dB. At 1 kHz, maximum intensity was limited at 60 dB by a large stimulus artifact. Opened stars are data from Kramer and Teas (1979).


1 kHz
2 kHz
4 kHz
8 kHz
VA
V
III
I
LATENCY (ms)
INTENSITY (dB HL)
10
9
8
7
6
8
7
6
5
6
5
4
3
2
1
0
40
50
60
70
80
90

difference for the 70 dB point. The plateau at 70 and 80 dB probably signifies that the wave I peak was confounded with signal artifact and/or CM. Since Kramer and Teas (1979) cancelled the artifact and CM, their 70 dB point is probably a better approximation of the true wave I latency. No data point could be obtained for the 90 dB level in the present study because of the very large signal artifact superimposed in the waveform (signal polarity was not alternated). At 8 kHz, there are no data points above 70 dB because of limited dynamic range due to the frequency response curve of the earphone. The greatest range of intensity was available for the 4 kHz FC. At high levels, the signal artifact was brief enough that it did not impose upon wave I. Note that as intensity is increased to the maximum level at 4 kHz, wave I latency continues to decrease and no plateau is evident, although there is a change in slope. At 1 kHz, wave I could not be reliably identified from noise for any S at 40 dB, and at 60 dB, the signal artifact imposed upon the wave I latency window.

The wave III data show a somewhat different pattern. Between 40 and 60 dB the lines are nearly parallel and above 60 dB they begin to converge. The slope of the latency change is inversely related to frequency. That is, the decrease in latency is greater for 2 kHz than for 8 kHz. At 90 dB all latencies are essentially equal across frequency.

Data points for wave V at 40 and 60 dB represent data pooled from the present study with Klein and Teas (1978). Before the data were pooled, mean latencies from the present study were compared to Klein's data. For the 1 kHz FC, 40 dB, wave V is 0.6 ms shorter in the present study, and at 60 dB, 0.2 ms shorter. The discrepancy at 40 dB is not surprising in view of the large variability (SD = .862 ms) in the data. Agreement at 2 and 4 kHz was quite good (within 0.1 ms). At 8 kHz, 40 and 60 dB, a 0.3-0.4 ms decrease in latency was found in the present study. This difference is quite large compared to the small variability (SD = 0.2 ms) at 8 kHz; therefore this finding is somewhat puzzling. At present no explanation is offered.

The latencies of wave I were subtracted from wave V at all stimulus conditions which had reliable data to observe how well wave V follows wave I. The results are shown in Table III. The missing data at 8 kHz are due to equipment limitations and at 2 kHz because of questionable reliability. No trend is evident either across intensity or frequency. Wave V in adults follows wave I very closely regardless of stimulus.

The large negative peak following wave V, labeled Wave VA, was included in the BSR analysis. This negativity was the largest amplitude wave in the BSR in many of the recordings, and at times, the only wave present at low intensity levels. Because the electrical configuration from which the BSR is recorded is a complicated one, response polarity was checked

TABLE III. Adult interwave intervals.

INTEN. (dB)	FC FREQ. (kHz) 2	4	8
WAVE I-V			
90	------	3.089	------
80	------	3.779	------
70	3.919	3.812	3.781
60	4.031	4.050	3.938
40	-----	3.799	3.884
WAVE I-VA			
90	------	4.651	------
80	------	4.624	------
70	4.647	4.622	4.869
60	5.054	5.170	4.920
40	------	5.165	4.876

The above differences are in ms.

by delivering a positive pulse to the active (G1) forehead terminal of the amplifier input. The amplifier output corresponded to an upward deflection for positive voltage at the input. The problem of polarity becomes important because wave VA, for example, could be interpreted as wave V. With the electrode configuration used in this study, forehead-positive corresponds to an upward deflection in the averaged response. There may be some question as to whether wave VA was what Jewett described as wave V. The latencies for the positive peaks I - V in the present study are somewhat longer (0.5 - 0.9 ms) in comparison with other studies (Jewett and Williston, 1971; Picton et al., 1974; Salamy and McKean, 1976), but if the latencies of the negative peaks are used, the values are quite discrepant, being about 3 ms longer than in other reports. A comparison of waveforms and recording configurations across various studies was made (Rowe, 1978; Chiappa et al., 1979; Starr and Hamilton, 1976; Salamy and McKean, 1976; Terkildsen, Osterhammel and Huis in't Veld, 1975; and Jewett and Williston, 1971). The present waveforms are similar to all except those shown by Jewett and by Salamy. Both these investigators show positivity plotted in an upward direction; however, their waveforms still appear inverted compared to those from the present study. Figure 5 is a BSR waveform taken from Salamy and McKean (1976). The most notable difference is that wave V in this report extends far below baseline (wave VA) and wave VI appears on the ascending slope of wave VA (Fig. 3). Salamy and Jewett show

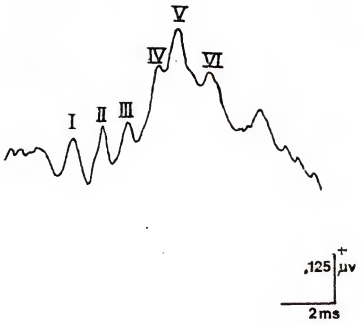


Fig. 5. Example of an adult BSR waveform taken from Salamy and McKean (1976). Waveforms similar in shape are also shown by Jewett (1971). Stimulus was a broad-band click presented at 55 dB sensation level, 15/s. Vertex positive activity is in the upward direction, as in the present study, however, the waveform appears to be inverted compared to those from Fig. 3.

little or no negativity after wave V, and wave VI appears on the descending slope of wave V. The shape of the BSR waveform depends upon many factors: the characteristics of the signal averager such as dwell time and number of points, variations in EEG filter settings (Terkildsen et al., 1975), acoustic stimulus (Klein and Teas, 1978), and wide individual differences under the same recording conditions (Chiappa et al., 1979).

Wave I-wave VA intervals were computed and can be seen in Table III. All intervals are similar except 4 kHz, 60 and 40 dB, and 2 kHz, 40 dB, which are slightly longer. However, since no definite trends are evident, wave VA will be assumed to be similar to wave V. Because of its large amplitude, wave VA may provide additional data when wave V is ambiguous.

The data points for all waves converge at high stimulus levels and have greater separation at the lowest levels. This is in agreement with other findings (Klein and Teas, 1978; Kramer and Teas, 1979; Elberling, 1976; Coats et al., 1979) and suggests that a more frequency specific response is available at lower intensity levels.

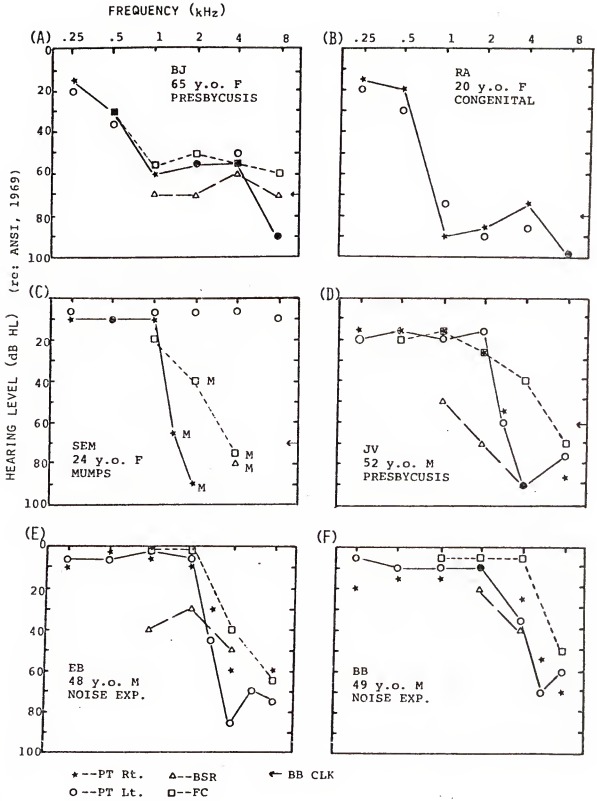
Hearing Loss Adults

Testing was attempted on 12 Ss meeting the criteria for hearing loss but only 6 were able to reduce ongoing electrical activity sufficiently to permit BSR recordings with the number of waveform rejections within an acceptable region (10%). The ages of the 12 Ss ranged from 20 to 65 years. No sedation was used.

Threshold Comparisons

Two sets of behavioral thresholds for the subjects with hearing losses are shown in Fig. 6. The circles (right ear) or stars (left ear) represent the pure tone (PT) thresholds and the squares represent thresholds to the filtered clicks (FC). Thresholds to FCs for subject RA (Fig. 6-B) could not be reliably determined (severe tinnitus interfered with the task). Thresholds to PTs for subject SEM could not be reached for 4 and 8 kHz (insufficient intensity was available). But note that the 4 kHz FC threshold was obtained at 75 dB HL and at 2 kHz, 40 dB HL. For subject BJ the differences between FC and PT thresholds were small except at 8 kHz. The FC threshold at 8 kHz was about the same as at 4 kHz, but the PT threshold at 8 kHz was 25 dB greater than at 4 kHz. The FC threshold was consistently lower than PT for all Ss. Energy in the FC below the center frequency appears to be effective in determining behavioral thresholds in the presence of sloping high-frequency hearing losses.

Fig. 6. Threshold audiograms for each hearing-loss subject. Each audiogram contains the subject's initials, age, sex, and cause of hearing loss. The circles and stars indicate pure tone (PT) thresholds for right and left ears, respectively. Squares indicate FC behavioral thresholds and triangles indicate BSR (physiological)threshold. The solid line indicates that the BSR and FC data refer to that ear. The small dashes connect FC thresholds and large dashes, BSR thresholds. The arrows at the right indicate level of BSR threshold to BB click. No entry means that no attempt was made to determine threshold. The M indicates that contralateral masking was used because of the possibility of acoustic crossover to the normal ear.


FREQUENCY (kHz)
(A) .25 .5 1 2 4 8
BJ
65 y.o. F
PRESBYCUSIS
(B) .25 .5 1 2 4 8
RA
20 y.o. F
CONGENITAL
HEARING LEVEL (dB HL) (re: ANSI, 1969)
0
20
40
60
80
100
(C)
SEM
24 y.o. F
MUMPS
M
(D)
JV
52 y.o. M
PRESBYCUSIS
(E)
EB
48 y.o. M
NOISE EXP.
(F)
BB
49 y.o. M
NOISE EXP.
*--PT Rt.
O--PT Lt.
Δ--BSR
□--FC
← BB CLK

For subjects with normal hearing it was determined that more acoustic energy is required for BSR threshold to FCs than for behavioral thresholds. The BSR thresholds to low-frequency FCs require more energy than high-frequency FCs. From normal-hearing adult subjects, wave V thresholds of 40 dB to the 1 kHz FC, and 10-20 dB to the 2, 4, and 8 kHz FCs are found (Klein, 1976; Klein and Teas, 1978).

Thresholds determined by BSR in the subjects with hearing loss are plotted in Fig. 6. The shape of the BSR audiogram is generally similar to the behavioral PT audiogram except that the BSR thresholds are higher. When a severe, high-frequency loss exists (at 8 kHz for BJ, at 4 kHz for SEM, and at 4 kHz for EB), the behavioral and BSR audiograms are no longer parallel. In these cases, BSR threshold is much lower than behavioral PT. In these cases it is likely that the threshold BSR originates from frequency regions below the frequencies of maximal hearing loss. If so, the frequency specificity of the BSR might be further examined by finding the highest frequency for that S at which PT threshold is normal, provided that the audiogram has no multiple peaks, and observing BSR threshold levels. These conditions occur at 0.5 kHz for RA, 1 kHz for SEM, and 2 kHz for JV, EB, and BB.

For RA no behavioral FC or BSR measurements could be obtained, a result which - in this case - is a positive finding, discussed later. Subject SEM had a similar loss except that her normal hearing range extended to 1 kHz with

PT thresholds decreasing rapidly to reach a 65 dB loss by 1.5 kHz. In this subject, 1 kHz FCs failed to elicit a BSR at a level of 60 dB HL. A BSR threshold was also unobtainable at 2 kHz even though the behavioral FC threshold was established at 40 dB HL. The only BSR to FCs obtained from SEM was found at 4 kHz which was within 5 dB of the reported behavioral one.

Subjects JV, EB, and BB have normal hearing extending to 2 kHz with thresholds increasing rapidly above 2 kHz. The 1 kHz BSR thresholds were normal for EB and slightly elevated for JV. BSR was not measured at 1 kHz for BB. At 2 kHz, EB's BSR threshold was 10 dB above normal (30 dB HL), JV's was 50 dB above normal (70 dB HL), and BB's was normal (20 dB HL). The hearing loss for BB is much less than for EB or JV, particularly at 3 and 4 kHz. At 4 kHz, BSR agrees better with PT threshold than with FC threshold for BB and JV, while for EB, BSR agrees better with FC threshold. The next section will examine these BSR-PT relationships more closely.

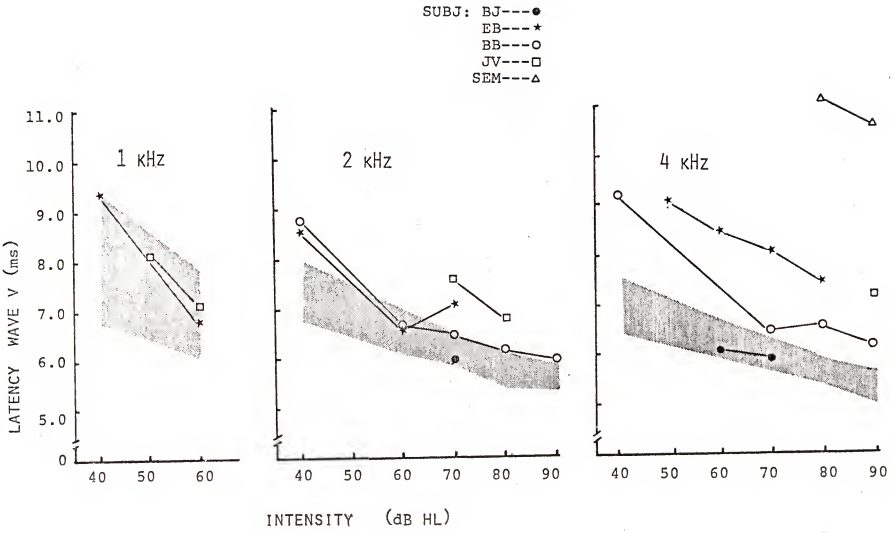
Latency Functions

The latency by intensity (L-I) functions of the hearing loss Ss can be compared to normals as another means of estimating the frequency regions along the cochlear partition that contribute to the BSR (wave V) since the frequency locations at which a severe hearing deficit exists should contribute minimally to the BSR. The relation between the latency of wave V and frequency was previously discussed. Waveforms from subjects with hearing loss were generally

smaller in amplitude than those from normal adults. This was most apparent for the peaks occuring before wave V since they were usually not present even to high-intensity, high-frequency stimuli, while wave V was observable. Therefore, only wave V latencies were measured. The latencies of wave V from subjects with hearing losses are plotted in Fig. 7. The shaded areas show the total range of wave V latencies previously observed in the normal adult group. The function at 1 kHz for EB and JV are within the normal range, and their PT thresholds were also normal at 1 and 2 kHz (Fig. 6). Latencies for BJ were difficult to determine at 1 kHz because her response waveform, unlike the other subjects, included a frequency-following component (FFR) (Moushegian, 1977) which obscured latencies. The FFR is not evident above 1.5 kHz. Responses at 1 kHz were not included. Subjects SEM and RA had no measurable 1 kHz BSR responses, and 1 kHz was not measured for BB.

At 2 kHz, EB, BB, and JV have normal PT thresholds as shown in Fig. 6. The latencies to 2 kHz FCs for BB are slightly longer than normal at 40 dB but fall within the normal range at higher intensities. The slope of the hearing loss between 2 and 4 kHz is much steeper for EB than for BB; however, their latencies are very similar at 40 dB. The increase in latency from 60 to 70 dB for EB is surprising and may indicate that the latency at 60 dB is underestimated, perhaps due to ambiguity of the wave V peak. At 70 dB the peaks are less ambiguous. Of the three subjects, JV has

Fig. 7. Latency-intensity functions for wave V from hearing-loss adults. The shaded areas represent the range (maxima and minima) of values obtained from the normal adults. The symbols for hearing loss Ss are identified in the legend.


SUBJ: BJ---●
EB---★
BB---○
JV---□
SEM---△
1 kHz
2 kHz
4 kHz
LATENCY WAVE V (ms)
11.0
10.0
9.0
8.0
7.0
6.0
5.0
0
40
50
60
70
80
90
INTENSITY (dB HL)

the largest amount of high frequency loss demonstrated by the PT audiogram. The 2 kHz L-I function for JV is somewhat different from the others; the BSR threshold was 55 dB above his normal 2 kHz PT threshold and wave V latencies are much later than normal. The latency at 2 kHz, 70 dB, matches the latency expected from normals to 1 kHz, 60 dB. A supra-threshold intensity series was not performed for BJ, but the threshold response is near the lower limit of the normal range.

At 4 kHz, the L-I function for BJ is in the normal range, but at 70 dB the latency at 4 kHz is equal to the 70 dB latency at 2 kHz. Subject BB's 4 kHz L-I function is above the normal range at the lowest intensity and approaches the normal range at high intensities. The 4 kHz function is very similar to that for 2 kHz except the latencies are slightly longer at 4 kHz than at corresponding dB levels at 2 kHz. Subject EB has an L-I function which parallels the normal range but does show a slight trend in approaching normal as intensity is increased. Only one data point was available for JV since the threshold response was obtained at equipment limits; however, this threshold latency lies approximately where the extrapolated latency for EB at 90 dB would be. The latencies at 4 kHz for SEM are extremely long. They are comparable to wave V recorded in normals to a 500 Hz FC presented at 40 dB HL (Klein and Teas, 1978).

In general, BSR thresholds to BB clicks were within 10 dB of the lowest BSR FC threshold; however, more data are needed before a meaningful comparison can be made.

Infants

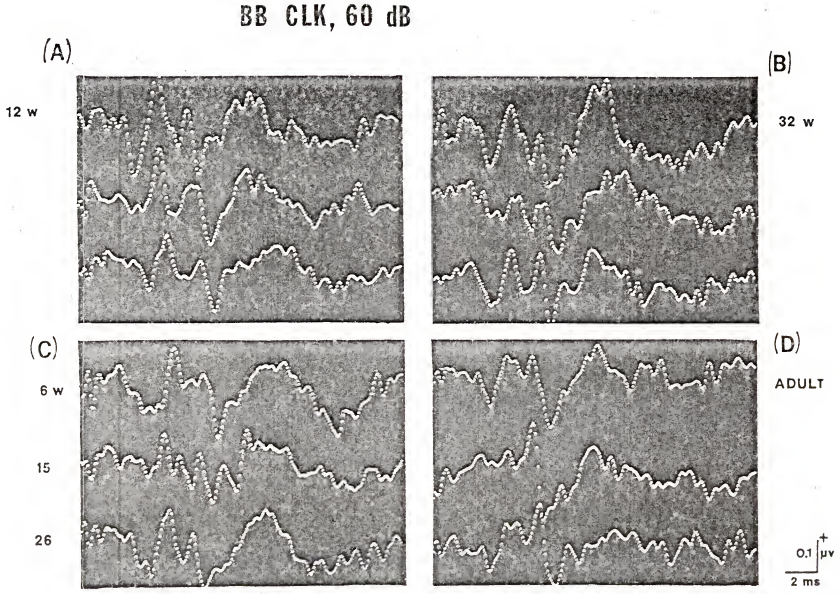
A total of 60 infants were tested, 25 males and 35 females. No sedation was used. Of this total, 6 would not sleep on one or more sessions and were eliminated from the study; 4 had very poor responses for undetermined reasons and were eliminated; 20 were tested once and then withdrew; thirty infants were tested longitudinally (more than once). Age was determined from date of birth to date of the experimental session in weeks. Three were from 2 to 4 weeks premature. Their data did not differ significantly from the term infants, therefore they were not differentiated from the rest.

Waveforms

The waveforms from infants in response to BB clicks were similar to those from adults, but some differences could be observed. Figure 8 shows waveforms from several infants and adults. Waveforms from 3 different 12-week olds are shown in Fig. 8A; 3 different 32 week olds in Fig. 8B; 1 infant tested longitudinally at 6, 15, and 26 weeks in Fig. 8C; and 3 different adults in Fig. 8D. The most obvious difference between the infant waveforms and those from adults is the large amplitude of waves I and III in the infant. Wave V-VA is the largest wave in adults, however, many times in infants wave III is larger than wave V.

Intersubject variability in waveforms from infants and adults can be observed in Fig. 8A, 8B, and 8D, and intrasubject variation across age in Fig. 8C. Intersubject variability within age groups appears to be less than intrasubject

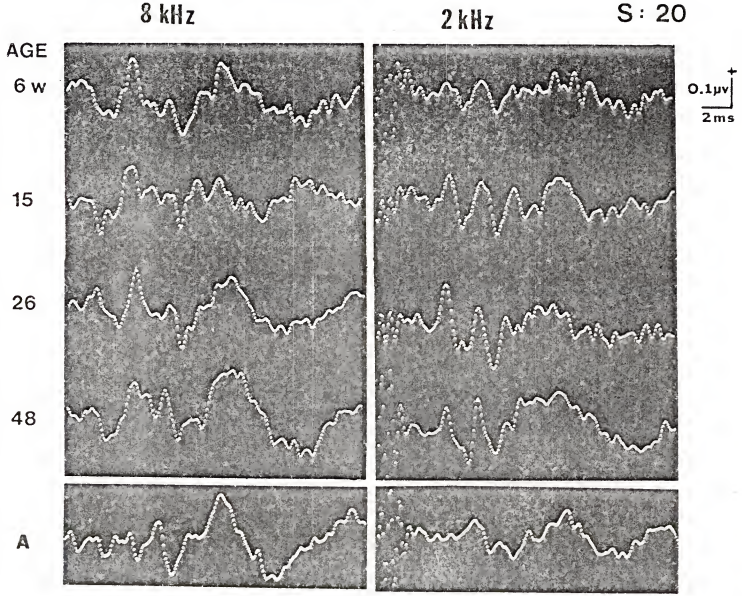
Fig. 8. Waveforms from infants and adults to a BB click presented at 60 dB, 30/s. Brainstem response waveforms from: (A) 3 different 12-week olds (subjects 25, 44, 45); (B) 3 different 32-week olds (subjects 13, 21, 29); (C) 1 infant (subject 20) tested at 6, 15, and 26 weeks; 3 different normal-hearing adults (subjects 2004, 2007, 2011).


BB CLK, 60 dB
(A)
12 w
(B)
32 w
(C)
6 w
15
26
(D)
ADULT
0.1 μv
2 ms

variability across age, i.e., age has the greater effect on waveform shape. Other investigators also report changes in waveforms produced by BB clicks with age. For example, Salamy and McKean (1976) reported that the infant BSR waveform contains only waves I and V at birth and waves II and III begin to appear at 6 to 12 weeks. Hecox (1975) shows a large wave III at 1 day of age which decreases in amplitude as age increases-- a finding consistent with the present study using FCs. It appears that there is a great deal of infant waveform variability from different laboratories as for normal adults, as described above. This situation precludes any meaningful attempt to address the question of different findings reported from different workers.

Waveforms to FCs change with FC frequency and age. The BSR to the 8 kHz FC in many of the youngest infants has a very robust wave III. Wave V is smaller, approximately equal in amplitude to wave I, or for some Ss, barely above noise level. As the infant matures, the amplitude of wave V increases and equals wave III by about one year. At the youngest ages, for the 1 and 2 kHz FCs, wave V is equal to or greater in amplitude than wave III, but the relation varies with individuals, while in adults wave V is nearly always larger than wave III regardless of stimulus. Representative waveforms for one infant tested longitudinally at 6, 15, 26, and 48 weeks, and an adult comparison, are shown in Fig. 9. The amplitude of wave V to the 60 dB, 8 kHz FC increases with age while for the 60 dB, 2 kHz FC, waves III and V are

Fig. 9. Brainstem response waveforms to FCs from infant and adult. Waveforms on the left are to an 8 kHz, 60 dB FC and those on the right, to a 2 kHz, 60 dB FC. The infant was tested longitudinally at 6, 15, 26, and 48 weeks as indicated on the left of the figure. The A indicates two waveforms from the same adult. See text for details.


8 kHz
2 kHz
S : 20
AGE
6 w
15
26
48
A
0.1μv
2ms

equal in amplitude at 6 weeks and remain equal as both waves increase in amplitude with age. As with BB clicks, the infant wave III at both frequencies is larger than the adult.

Table IV shows the relative frequency of detecting each BSR component for each stimulus over the entire sample of observations from 4 to 48 weeks. The numbers in parentheses are adult values. Over the entire age range the probability of detecting a response (POR) increases with center-frequency of the FC. Wave I is not detected at all for the 1 kHz FC at either 40 or 60 dB, but more than 75% of all opportunities yielded a wave I for the 8 kHz FC. At the 60 dB intensity, responses to the 4 kHz FC were less likely to be detected than to the 2 or 8 kHz FCs. At 40 dB there is a highly systematic increase in POR of BSR components as FC frequency increases. However, at 60 dB, waves III, V, and VA are detected about equally for the different FCs.

The adult values essentially follow the same trend as infants; however, the POR is usually slightly higher with adults. This is most pronounced to the 1 kHz, 40 dB FC where wave III in infants has a POR of .21 compared to .70 in adults.

Effects of Age on Latency (Cross-Sectional)

Infants were grouped by age, over 2-week intervals from 4 to 19 weeks, 4-week intervals from 20 to 35 weeks, and a final group at 46-48 weeks. Some of these infants were followed longitudinally, and others were tested only once. Latencies of waves I, III, V, and VA *vs* log age in weeks were

TABLE IV. Probability of detecting a BSR component in infants and adults.

	60 dB				40 dB			
FREQ	I	III	V	VA	I	III	V	VA
BB	0.84 (0.73)	0.97 (0.73)	0.99 (1.00)	0.94 (1.00)	N.A.			
8 kHz	0.82 (0.67)	0.94 (0.89)	0.97 (0.95)	0.97 (1.00)	0.78 (1.00)	0.97 (1.00)	0.98 (0.94)	0.95 (1.00)
4 kHz	0.37 (0.67)	0.66 (0.78)	0.84 (1.00)	0.87 (0.78)	0.42 (0.50)	0.68 (1.00)	0.90 (0.89)	0.82 (0.88)
2 kHz	0.44 (0.40)	0.78 (1.00)	0.98 (0.95)	0.84 (0.90)	0.28 (0.11)	0.55 (0.67)	0.86 (0.90)	0.74 (0.80)
1 kHz	N.A. (N.A.)	0.70 (0.73)	0.90 (0.95)	0.85 (0.73)	N.A. (N.A.)	0.21 (0.70)	0.65 (0.80)	0.56 (0.78)

Values in () are from normal adults

plotted in scattergrams for each of the 9 stimulus conditions. The data for 2-week intervals were plotted at the upper week, and the data for 4-week intervals, at the midpoint of the interval. Linear regression curves ($Y = m \log X + b$) were computed from the latencies for each wave along with the standard error of estimate (SE) and are displayed in Figs. 10-18. Adult mean latencies and $\pm$ 1 SD are shown at A on the abscissa. Also entered in association with each curve are 1) the regression equation, 2) the number of responses obtained out of the total number of attempts, and 3) the Pearson linear correlation coefficient (r). The asterisk indicates that the correlation is significantly ($p < .05$) greater than zero.

The only significant correlation for wave I was found for the 2 kHz FC at both 40 and 60 dB (Figs. 15-16). There was no indication of significant changes in wave I latencies with age for the 4 and 8 kHz FC or BB click at either 40 or 60 dB. From the present data it appears that wave I latency is equal to adult latency by 5 weeks of age to 4 and 8 kHz FCs and to BB clicks. For the 2 kHz FC, there is a decrease of latency with age. This decrease appears to asymptote, for both levels, at about 15 weeks under visual inspection of the figures; however, the regression line does not reach the adult mean until about 30 weeks. The 40 dB adult data point, obtained at a stimulus repetition rate of 10/sec, might occur at a shorter latency than points obtained at 30/sec. At 40 dB, the wave I data point for adults was taken from Kramer and Teas (1979) because of the difficulty in obtaining the response

Figs. 10-18. Effect of age and stimulus frequency on latency of waves I, III, V, and VA. Each point represents one latency measurement. The solid lines represent the best-fit regression described by the equations. Below the equations are entered: r, the correlation coefficient, and, number of responses detected/number of opportunities. Asterisk (*) indicates r is significant ($p < .05$). The dashed lines indicate ± 1 SE. On the abscissa, age is represented logarithmically; A indicates adult target latencies with bars showing ± 1 SD. Stimulus conditions are indicated at the top of the figures.

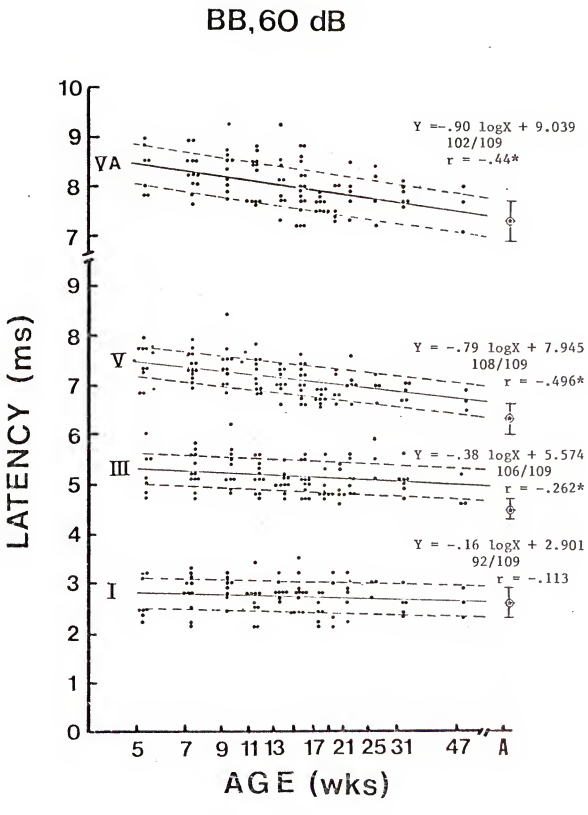


Fig. 10. Age effects to BB, 60 dB. See legend on page 67.

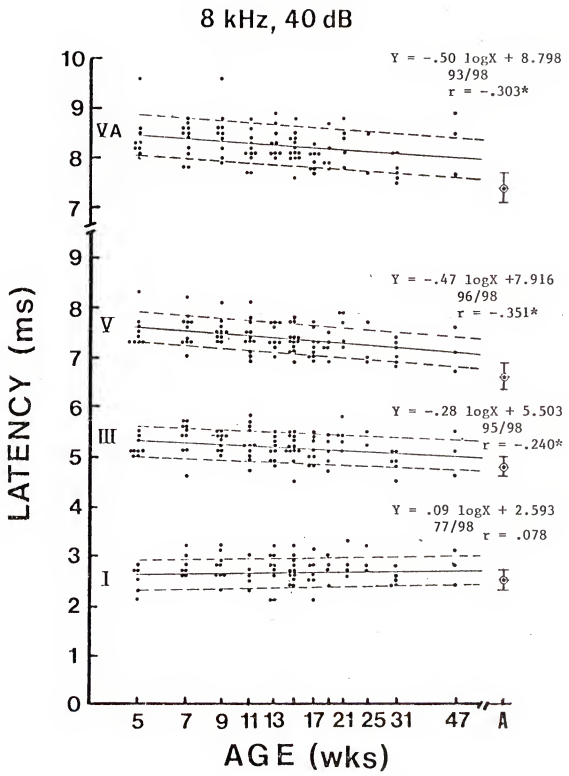


Fig. 11. Age effects to 8 kHz, 40 dB. See legend on page 67.

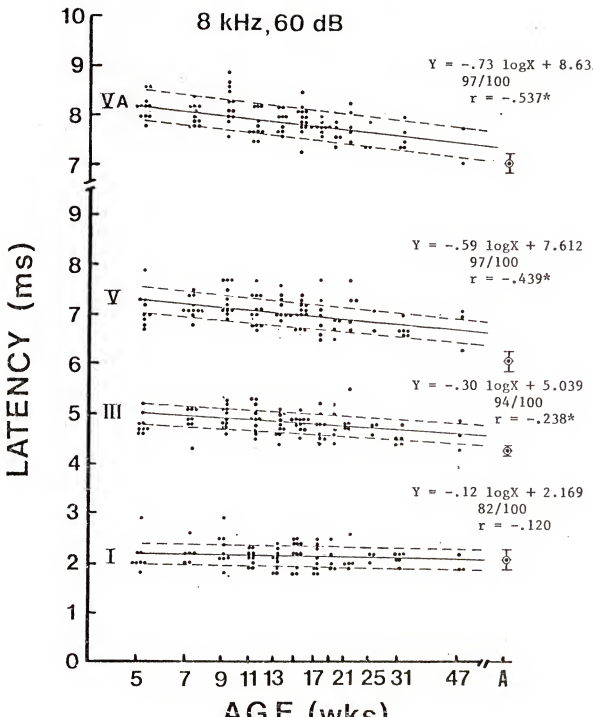


Fig. 12. Age effects to 8 kHz, 60 dB. See legend on page 67.

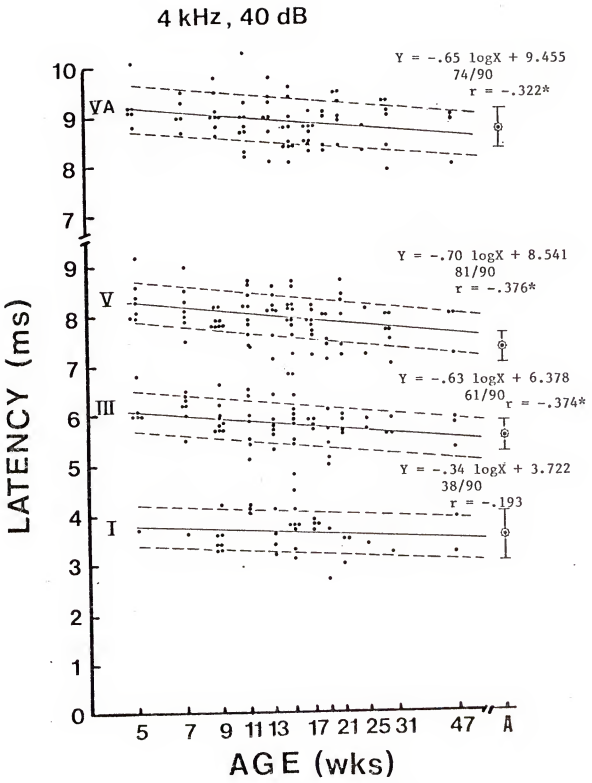


Fig. 13. Age effects to 4 kHz, 40 dB. See legend on page 67.

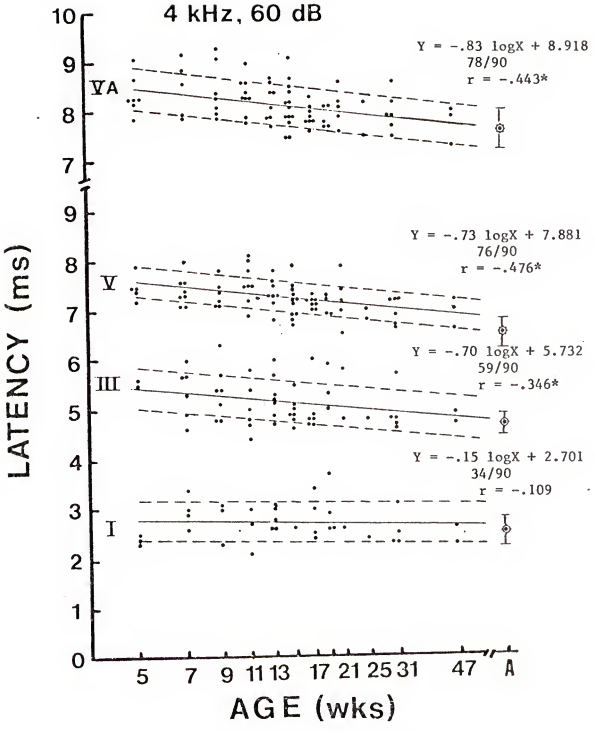


Fig. 14. Age effects to 4 kHz, 60 dB. See legend on page 67.

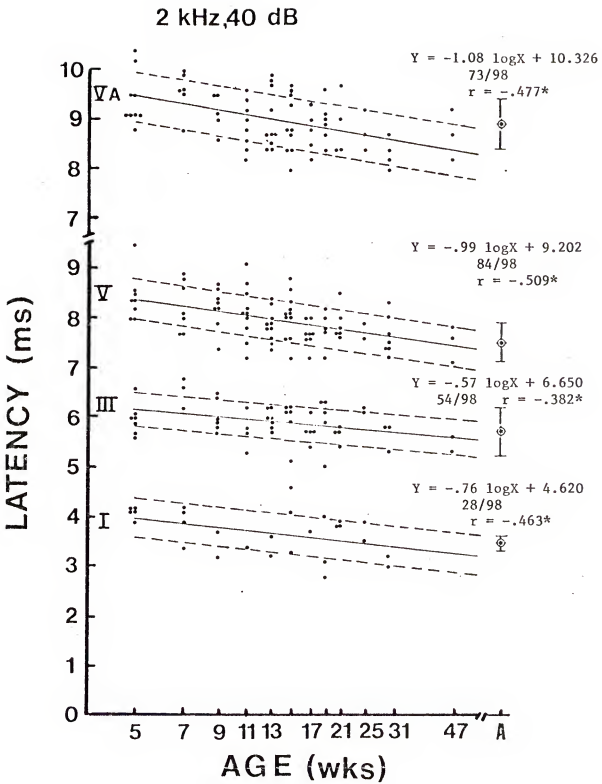


Fig. 15. Age effects to 2 kHz, 40 dB. See legend on page 67.

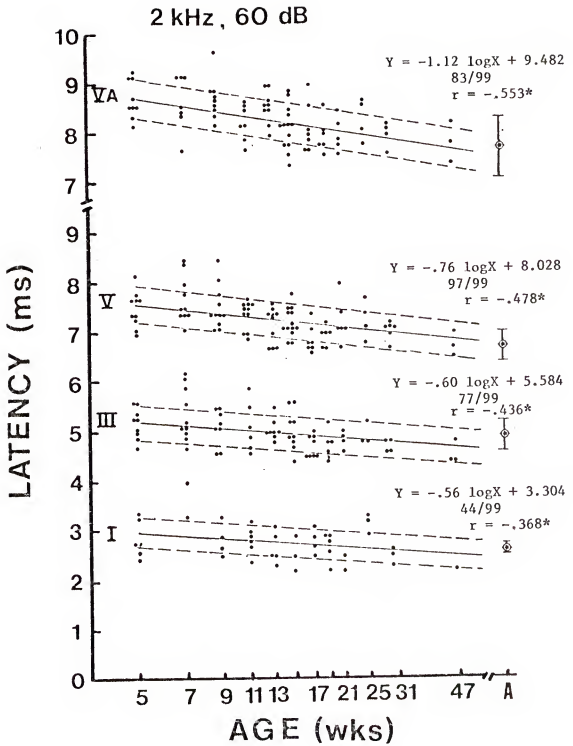


Fig. 16. Age effects to 2 kHz, 60 dB. See legend on page 67.

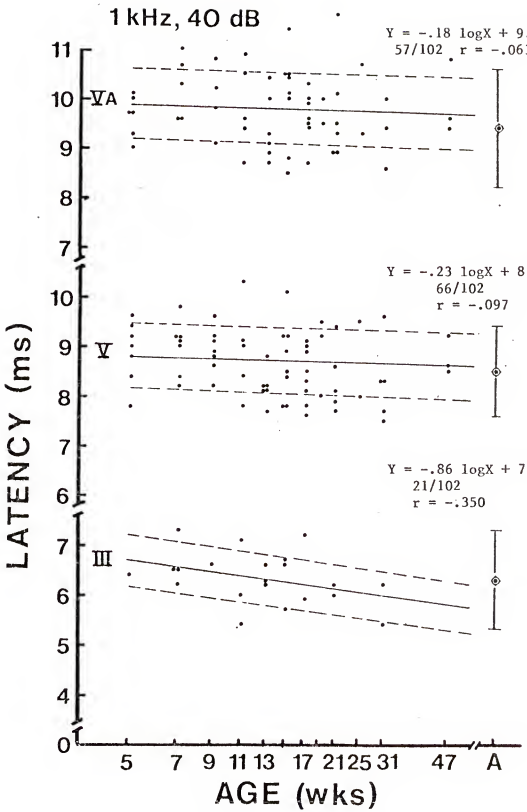


Fig. 17. Age effects to 1 kHz, 40 dB. See legend on page 67.

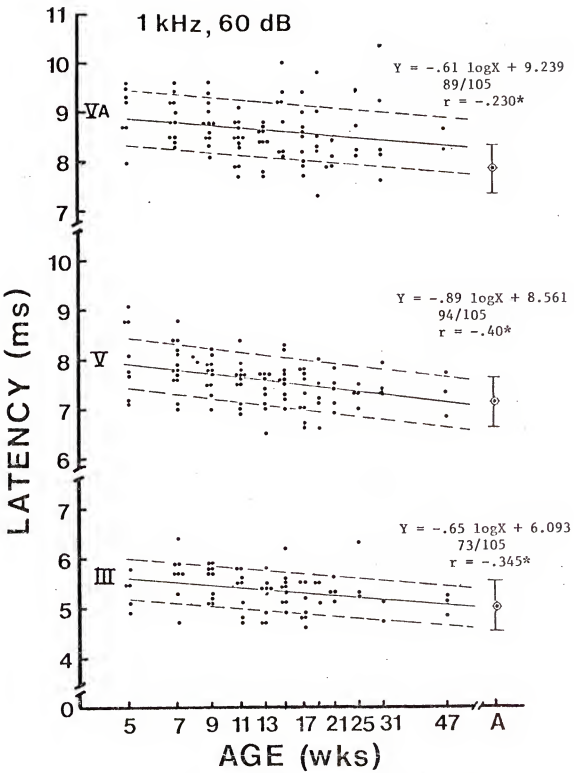


Fig. 18. Age effects to 1 kHz, 60 dB. See legend on page 67.

from the present recordings. In infants, the PORs for wave I, at 2 kHz 40 and 60 dB are .28 and .44, respectively. It may be inappropriate to make infant and adult latency comparisons at 40 dB because of the small number of data points. Since a significant correlation between latency and age suggests that a maturational process underlies the latency decrease, one should expect more infant response latencies longer than the adult (mature) value and fewer at latencies shorter than the adult value. For wave I, 2 kHz, 40 and 60 dB HL, the X^2 did not permit the rejection of a 50-50 split around the adult latency ($p=.05$). For wave III the $H:p = 0.5$ could be rejected for 2 kHz, 40 dB but not at 60 dB. The nonparametric, sign test was then used to test the same null hypothesis ($H:p=0.5$) and the same outcomes were found. Thus, the possibility that the latencies of waves I and III to 2 kHz FCs are age-independent cannot be ignored.

The regression lines of waves I, III, V, and VA show a trend of decreasing slope with increasing frequency. These data are summarized in Fig. 19 where slopes from the regression equations vs FC frequency are plotted for 40 and 60 dB levels. The parameter is BSR peak. For each stimulus condition, the amount of slope usually increases with the order of occurance for the waves, i.e. wave I has the smallest slope followed by wave III slope, wave V slope, and wave VA slope. Exceptions are wave VA at 1 kHz, 60 dB; wave I at 2 kHz, 40 dB; waves V and VA at 1 kHz, 40 dB. The slopes at 1 kHz, 40 dB are not significant; therefore, the slope of

Fig. 19. Slope of latency change due to age as a function of FC frequency. Data points for the BB click are shown at extreme right. The parameter is BSR wave. Values for rate of change (slope) were obtained from the regression equations in Figs. 10-18. Data at 40 dB are on the left and 60 dB on the right. Those symbols with N indicate slopes were not significantly different from zero.

40 dB
60 dB
WAVES
I
III
V
VA
SLOPE
-1.0
-0.9
-0.8
-0.7
-0.6
-0.5
-0.4
-0.3
-0.2
-0.1
0.0
+0.1
1
2
4
8
BB
N
FC FREQUENCY (kHz)

wave III, being larger than V and VA is probably not real, but rather a reflection of the large variability in the data. The significant slope for wave I at 2 kHz, 40 dB is based on 28 observations (POR=0.28) whereas, the significant wave III regression at 2 kHz, 40 dB is based on 54 observations (POR= 0.55).

At 60 dB, slopes for waves V and VA at 4 and 8 kHz tend to be larger than at 40 dB. The result is that the function for wave V and VA across frequency is shallow at 60 dB and steep at 40 dB. When infant and adult latencies are compared for wave V at 4 and 8 kHz, the deviations at 60 dB are greater than at 40 dB.

Regression equations for the BB click (Fig. 10) were compared to those of FCs. The closest agreement for slopes, Y-intercepts, and adult target latency values, was with the 4 kHz, 60 dB data (Fig. 14). The one major difference between these two curves was slope of wave III (-.38 for the BB click, and -.70 for the 4 kHz FC). The spectra of the 4 kHz FC and BB click are probably similar because the BB click contains most of its energy in the 4 kHz region as a result of the filtering effects and resonances of the transducer (TDH-39) (Davis, 1976) therefore the above findings are not surprising.

Latencies for all waves in infants and adults to the 8 kHz, 60 dB FC are shorter than to the BB click at 60 dB.

Although many of the correlations were significant, only a small percentage of the total variation is accounted for by

age alone. The largest coefficient of determination (r^2) is for wave VA at 2 kHz, 60 dB, and this only contributes 31% of the total variance to age. Observation of the data suggests that intersubject variability is responsible for most of the variance.

Effect of Age on Latency (Longitudinally)

Data from six of the longitudinal infants were compared with the computed regression lines and SE from the group data in the previous section. Figures 20-23 show results for the 8 and 2 kHz FC at 40 and 60 dB. As age increases, the data points tend to cluster more closely around the regression line for all stimulus conditions. Over repeated measurements on the same individual the latencies in relation to the regression line are consistent across stimulus conditions and waves. For example, the latencies for subject 21 are below the regression line for every wave, to every stimulus condition and this pattern is maintained across the age range studied. On the other hand, the data points for subject 19 cluster around the regression line being either slightly above, below, or right on it. This figure suggests that although there is much intersubject variability, intrasubject variability is small. For the 2 kHz, 40 dB FC only one out of the six subjects had a recordable wave I (POR=0.17) but note that the response for this S was recordable on every session. Thus, if a response is obtained on one session, the longitudinal observations suggest that, in future sessions, it will also be detected. If no response is recorded at one session, it will probably not be detected in future sessions.

Figs. 20-23. Individual longitudinal data compared to the group regression. The solid lines are the regression lines previously shown in figures with corresponding stimulus conditions. The dashed lines show ± 1 SE. Symbols represent measurements from 6 infants taken at various ages indicated by abscissa. Stimulus conditions are shown at the top of the figures.

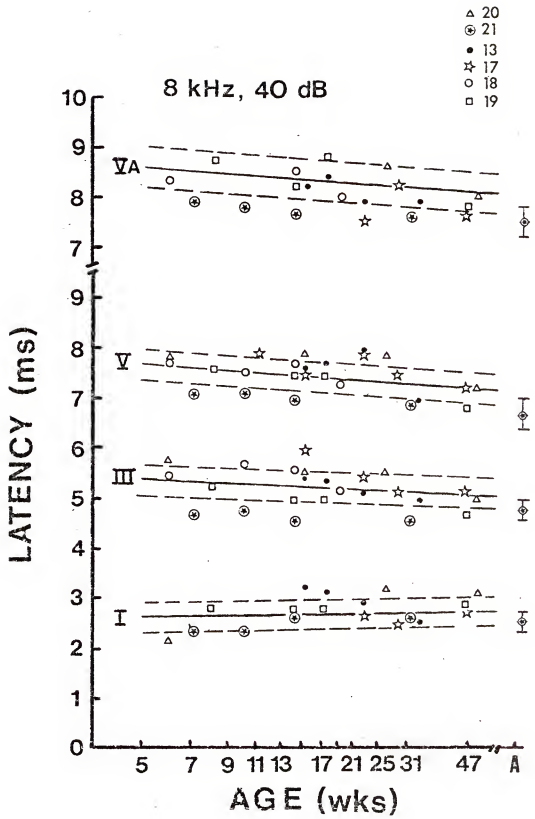


Fig. 20. Longitudinal data, 8 kHz, 40 dB.
See legend on page 82.

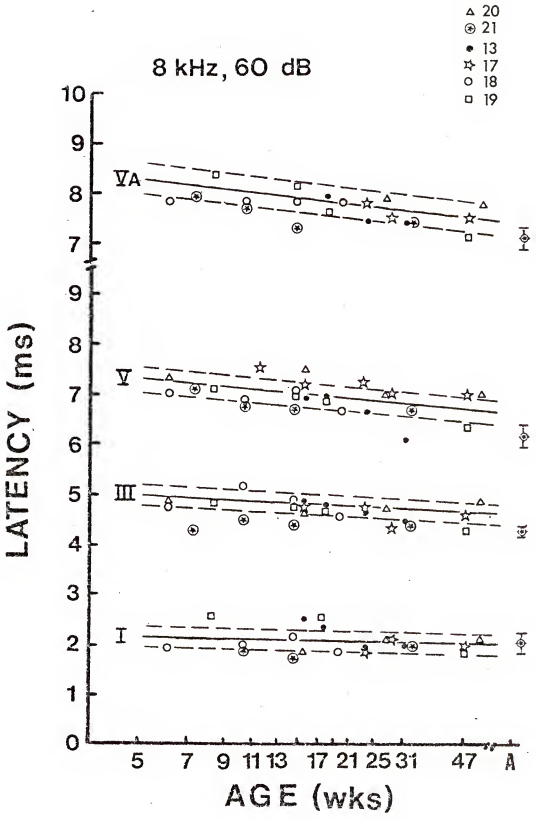


Fig. 21. Longitudinal data, 8 kHz, 60 dB.
See legend on page 82.

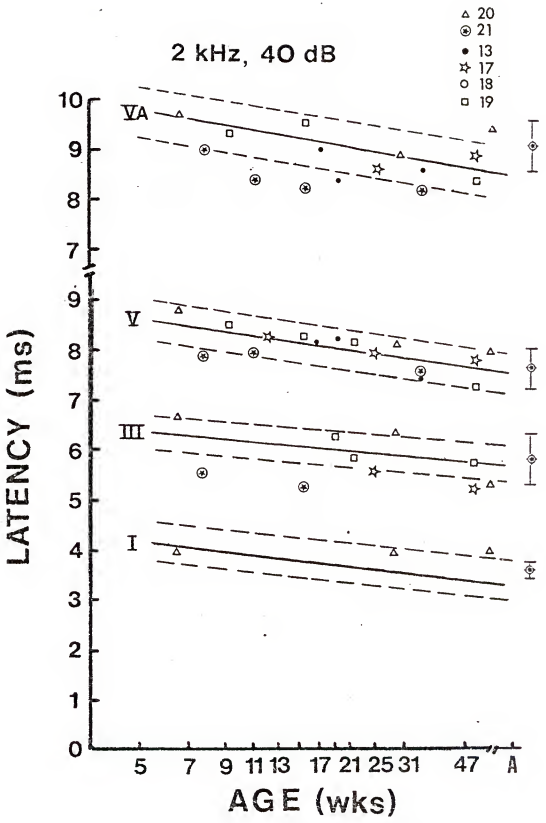


Fig. 22. Longitudinal data, 2 kHz, 40 dB.
See legend on page 82.

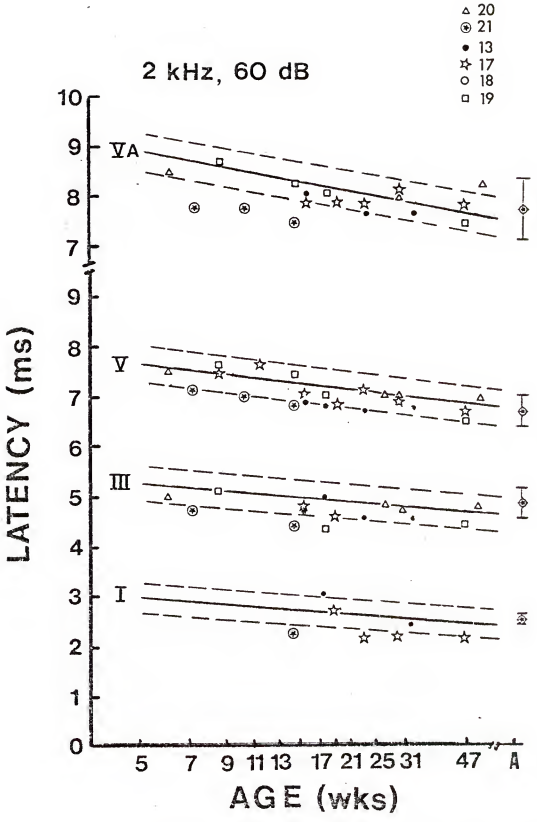


Fig. 23. Longitudinal data, 2 kHz, 60 dB.
See legend on page 82.

Intensity Effects

The change in latency of the BSR waves across intensity was observed for the 4 kHz FC because of the intensity range available. Levels of 40, 60, 70, 80, and 90 dB HL were presented to 5 infants: 1--4-week, 3--17-week, and 1--46-week old. These data, along with the normal adult means, are presented in Fig. 22. The data at 17 weeks are the means of the three subjects.

Infant and adult data are essentially superimposed for the wave I function. The functions for wave III are separated, with the youngest infant deviating most from the adult and the oldest deviating least. All functions for wave III are nearly parallel up to 70 dB at which point the curves plateau at 4 weeks, that is, latency remains constant from 70 to 90 dB. For wave V, the curves for infants deviate from the adult to a greater degree than for wave III. At 40 dB, all infant wave V latencies are equal, and as intensity is increased, the functions separate. The functions plateau for the 4-week old at 60 dB, and at 70 dB for the 17-week old. The decrease in latency with increase in intensity for the 46-week old does not plateau; however, the slope of the change is not as steep as with adults. This figure demonstrates that low-level stimuli at times may not effectively differentiate between infants of different ages even though there are differences between the adult group.

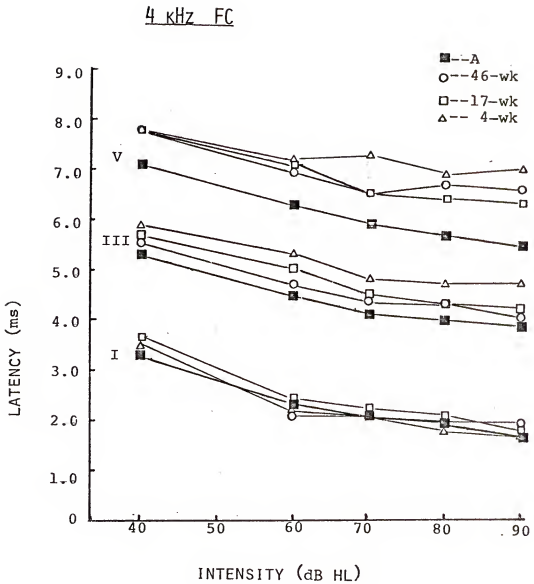


Fig. 24. Effect of intensity on latency of waves I, III, and V. Stimulus was a 4 kHz FC presented at 30/s at the levels indicated at data points. Stimulus levels are re: normal adult behavioral thresholds. Dark solid lines are normal adult intensity functions and the light lines are infants: l--4-week old; the mean of 3--17-week olds; l--46 week old; identified by symbols on the figure.

CHAPTER IV
DISCUSSION

In Chapter III data were presented from normal adults, adults with hearing loss, and normal infants. The focus of this study is on infants. The data from normal adults provide a standard for the mature ear to which infant responses can be compared. The adult data from persons with pure-tone losses afford another comparison for recognizing limitations in interpretations of the BSRs to FCs.

The waveform of BSRs and the latencies of the peaks within the waveform vary with center frequency of the FC, stimulus intensity, audibility curve, and age of the subject. The effect of age on the responses from infants appears to be complicated and varies depending upon BSR peak. Wave I showed no change in latency with age for the high-frequency FCs at 4 and 8 kHz; however, there was a decrease in wave I latency for the 2 kHz FC. In contrast, the wave V peak in response to the 4 and 8 kHz FCs showed a latency decrease with age, but, for the 1 kHz FC, the latency of wave V did not change with age. Although the wave III response was detectable for 1 kHz, and these latencies decreased with age according to the slope (-0.86), the correlation between latency and age was not statistically different from zero.

Unlike the infant sample, the BSRs from adults with hearing losses failed to show waves I and III prominently enough to measure, therefore only wave V was available for comparisons. The assumption is made that, in the adult, wave V parallels at a central site, the physiological output that arises in the cochlea. Such an assumption does not appear to be valid for infants (see Fig. 24).

PT Threshold and BSR Representation

In normal Ss the latencies of waves I, III, V, and VA were shown to vary greatest with center frequency of the FC when presented at low intensities (Klein and Teas, 1978). This finding was also assessed on a group of adults with hearing loss. The relations between PT audiogram, BSR threshold, and latency were examined for subjects with steep, high-frequency hearing losses. Several studies have now shown that as stimulus level is increased, N_1 and wave V responses originate from cochlear regions more basally located containing nerve fibers which have best thresholds for high-frequency stimuli (Eggermont, Spoor, and Odenthal, 1976; Elberling, 1976; Klein and Teas, 1978; Kramer and Teas, 1979). As stimulus intensity is increased, a wider area of the cochlear partition extending towards the base is stimulated. The evoked potential (BSR) becomes visible above the ongoing physiological noise when enough neural tissue is synchronously stimulated. Subjects with hearing loss required more stimulus energy to obtain a threshold evoked potential. This finding is consistent with the inference

that there is less responsive neural tissue available along the cochlear partition so that a wider region of the partition must be stimulated to produce an identifiable response. Furthermore, there should be a parallel between the amount of responsive area of the basal turn and the amount of hearing deficit. One can expect that the neural activity originating from the highest frequency region available dominates the gross evoked potential recorded from extra-cochlear electrodes (Teas et al., 1962) and because of the frequency X distance relation along the cochlear partition, latencies will be shorter, as the stimulated areas extend toward the base. Results from subjects with hearing loss at frequencies where PT thresholds are normal but hearing loss exists at slightly higher frequencies show that: (1) BSR - determined FC threshold may be elevated; (2) wave V latency at the elevated BSR threshold may be longer than normal. These findings are probably the result of the restricted responsive region along the cochlear partition defined by the PT audiogram. In many cases, BSR-determined FC threshold corresponded well with the PT threshold in the deficit area 1/2 to one octave above the frequency of the FC depending on intensity level. These findings suggest that in normal-hearing Ss, cochlear locations basal to the center-frequency of the FC contribute significantly to the BSR, even when FCs are presented at intensities as low as 40 dB HL. If one adds a correction factor of about 1/2 octave to the center frequencies of FCs

presented at 40 dB, and about one octave for 60 dB, the results more accurately parallel the PT threshold measures. This correction factor is consistent with the findings of Kramer and Teas (1979). They showed that wave V latency to a 2 kHz, 40 dB FC presented with simultaneous, selective, high-pass masking remains unchanged until the low-frequency cutoff of the masker is lowered to 3 kHz. When the masker was at 3 kHz, wave V latency increased suggesting that this cochlear region contributes significantly to BSR recorded to the 2 kHz, 40 dB FC. Furthermore, the data from subject RA suggests that BSRs cannot be obtained from apical cochlear locations responsive to PTs below approximately 750 Hz.

Waveforms

For all stimulus conditions in which wave I could be recorded, its amplitude in infants was larger than in adults, however, this relation was not measured in detail. The skull of the infant contains many areas of incomplete ossification, or fontanels; one fontanel is located in the mastoid region. As the skull ossifies, the neuroelectric activity from the brain, recorded at the scalp, can be attenuated. The electrodes may be closer to the source of the potential in infants and the orientation of the electrical field with respect to the electrodes also may be different resulting in a larger signal at the scalp electrode.

Wave III was also observed to be large in amplitude which decreased with age. Some anatomical support for the large wave III response in infants may come from the report

by Strominger and Hurwitz (1975) describing SOC cells in human infants as more numerous, larger, and more densely packed than those found in the adult. It is speculative as to whether all SOC cells in the infant are functional, but if they are, one might expect a more synchronous gross response composed of more neural elements, hence, a larger-amplitude evoked potential. As the organism matures, the SOC differentiates and enlarges, cell density decreases, and the number of cells decreases perhaps due to normal attrition with age. Each peak in the BSR has been reported to represent activity from successive auditory brainstem nuclei (Jewett and Williston, 1970; Buchwald and Huang, 1975; Starr and Hamilton, 1976); however, activity from multiple adjacent sources can produce complicated resultants due to additive effects within the gross response recorded from the scalp. Activity from neural masses adjacent to the source of wave III could make wave III larger in infants than in adults if orientation of the electrical fields are different. The age at which the infant wave III decreases to adult values is sometime beyond the age range covered in this study.

Wave V amplitude increased with age. The greatest change was seen to the 8 kHz FCs which produced very low-amplitude wave Vs in the youngest infants. The amplitude of wave V to 2 kHz FCs increased slightly with age and many times it exceeded the response to 8 kHz FCs from the same infant; this was never observed in adults. Since amplitude was not

studied quantitatively, it cannot be determined at what age wave V is equal in amplitude to adults, but a qualitative appraisal of the waveforms suggested that wave V amplitude to 2 kHz FCs equals adults quite early in the age range studied, while to 8 kHz FCs, adult amplitude may not be obtained until sometime after one year. The wave V potential is thought to be correlated with activity from the inferior colliculus (IC) (Buchwald and Huang, 1975; Starr and Hamilton, 1976). If future research proves this interpretation correct, then changes in wave V would be one measure of maturation of the IC. Increasing amplitude of V may reflect a progression in nerve fiber myelination and an increasing number of active neural elements. Rorke and Riggs (1969) showed that the IC in human neonates has few myelinated fibers. In kittens, Aitkin and Moore (1975) found predominantly low characteristic frequency (CF) units with very few high CF units when recording from the IC. These findings may support the present data on wave V to FCs suggesting the possibility of a low- to high-frequency (tonotopic) maturational pattern in brainstem auditory pathways.

Latency

Adults

The normal adult latency-intensity functions (L-I) (Fig. 3) indicated that at the highest intensity, all latencies regardless of stimulus frequency, are equal to the 8 kHz latency for each respective wave. This confirms the prediction by Klein and Teas (1978) who showed a trend

for latency convergence at the highest intensity (60 dB HL). Thus, stimulus intensities produce brainstem potentials which originate from most basal cochlear locations irrespective of stimulus frequency; frequency resolution is lost at strong intensities. The lowest stimulus level provides the greatest frequency resolution, but with a lesser probability of obtaining a response and a larger variance.

Results from this study showed that normal adult BSR waves I, III, V, and VA maintain a fairly constant interpeak time interval for all stimulus conditions. The range of wave V-I intervals across all stimulus conditions covers about 0.5 ms which may be within the expected variance. In an earlier report (Klein and Teas, 1978) it was suggested that the wave V-I interval may decrease as frequency is decreased. This is not supported in the present findings. Coats et al. (1979) reported finding that the wave V-N_1 interval is intensity and frequency dependent. At low intensity, the interval is about 1.8 ms to a 1 kHz FC and 4.3 ms to a 8 kHz FC. At high intensities, the 1 kHz wave V-N_1 interval is 3.8 ms, and 4.1 ms at 8 kHz. Kramer and Teas (1979) reported that the wave V-N_1 interval to a 70 dB, BB click is 0.36 ms longer than to a 40 dB, 2 kHz FC. Both Coats et al., and Kramer and Teas used an ear canal electrode to record N_1. This electrode provides a more detailed view of the VIII nerve response (N_1) and may be more sensitive to slight latency changes than wave I. For purposes of the present study, it will be assumed that the wave V-I interval is constant across stimulus parameters.

Infants

The age-related changes in latency in BSRs from infants vary with BSR peak. In general, the latency of wave I to high-frequency FCs does not change with age while the latencies of wave V peaks do. This is consistent with other findings (Salamy et al., 1975; Salamy and McKean, 1976). However, for the 1 kHz FC, wave V latency does not change with age. Wave I is not detectable to the 1 kHz FC, and although 2 kHz does elicit a wave I, its POR is 0.29, and the variability is higher than for 4 or 8 kHz. The correlation between latency and age for wave I to the 2 kHz FC was significant, however.

Thus, for high frequencies the data show a caudorostral sequence of maturation. Low frequencies are clearly different, both at wave I and wave V, from high frequencies. The increase in variability of wave I latency for the responses to the 2 kHz FC also suggests caution in close interpretation. Since the later BSR peaks show clear evidence of maturational, or age-related latency decreases, inferences about cochlear maturational changes should be based on the earliest peaks available, viz, in this study, wave I. However, the low-frequency FCs elicit wave Is with low PORs and high variability. The later peaks, in particular wave V, are elicited with PORs comparable to adults. Therefore, the high-frequency FCs produce a full complement of BSR peaks (waves I, III, and V) and the low-frequency FCs produce only waves III and V. Table V represents a ranking of confidence in

TABLE V. Reliability rating of BSR peaks.

FREQ. (kHz)	WAVES I	III	V
8	++	++	++
4	++	++	++
2	-	+	++
1	--	-	+

++ Excellent, POR > 0.8
+ Good, POR > 0.5
- Fair, POR > 0.2
-- Poor, POR < 0.1

the reliability of BSR peaks based principally on the POR but also the interpretation of the experimenter. From these rankings one can see that inferences about cochlear maturation based on wave I latency must be made cautiously since the full frequency range is not available. The present data show that broad statements such as, "BSRs from infants show the presence of a high-frequency hearing loss" may be incorrect. The high-frequency FCs produce wave I responses with latencies that are similar to adult values; the lag in latencies is shown to occur at central, not at peripheral sites. The problem appears to be more complicated than broad statements like that above imply. Even though waves III and V in response to high-frequency stimuli show a developmental trend progressing toward adult values, the wave V latency to the 1 kHz FC is similar to the adult value and does not decrease with age. One might then assume that the responsive high-frequency regions at central sites (V) are undergoing developmental changes (even though cochlear regions are not) but that the central regions responding to low frequencies are mature. In this view, one might assume that the entire cochlear partition is fully mature and is responding as in the adult. However, the wave I data at 2 kHz, while showing a low value for POR, are still suggestive of a relation between latency and age. While these changes might be due to cochlear maturation, developmental changes in the external canal and middle ear might alter their resonance and result in a progressive increase in effective

intensity at the stapes leading to a decrease in latency with age due to intensity. Even though the latency decreases at 2 kHz might be due to changes in intensity, the apparently mature wave V response at 1 kHz 40 dB presents a problem in interpretation that is similar to a paradox observed and addressed by others. Consistent findings in animal preparations (kittens and chicks), whether recording from the round window and CN (Brugge, Javel, and Kitzes, 1978; Saunders et al., 1973), the IC (Aitkin and Moore, 1975), or the cortex (Pujol and Marty, 1968) are that responses to predominantly low-frequency stimuli are obtained at the earliest ages with high-frequency responses occurring later in the development cycle. The paradox is that these low-frequency responses are obtained even though apical cochlear regions maximally responsive to those frequencies are poorly developed. Basal regions, usually responsive to high-frequency stimuli, are quite mature, yet few high-frequency physiological and behavioral responses are obtained. No solid explanations have been offered. Perhaps Pujol summed up the situation when he wrote "These characteristics of the beginning of sound sensibility (sic) may perhaps lead to the reconsideration of certain aspects of the physiology of hearing in adult mammals..." (Pujol and Marty, 1968). A major difference between the human infant and animal studies is that in animals, the VIII th nerve response is best recordable to low-frequency stimuli and difficult to elicit to high frequencies, while in infants, wave I has normal responsivity to high frequencies.

A possible explanation in support of the immature-cochlear hypothesis could be that low frequencies are transduced in the mature basal turn; however, one still must account for the absence of an age effect to 1 kHz 40 dB FCs. It is possible that there is an age effect, but it is obscured by the large variability of the data. At 1 kHz, 60 dB, there is a small but significant age effect on waves III, V, and VA though it cannot be determined if this is due to central and/or peripheral maturation without wave I data. More basally located fibers can be stimulated by the 1 kHz FC presented at 60 dB than at 40 dB, therefore, the latency change with age seen at 60 dB may be due to stimulation of the same tissue primarily responsive to high-frequency stimuli.

The frequency and age effects on wave III and V are consistent with a tonotopic maturational sequence in the CAS. The data suggest that pathways in the CAS which carry low-frequency information reach maturation before high-frequency pathways. The decrease in wave V latency with age to BB clicks has been previously observed (Salamy et al., 1975; Salamy and McKean, 1976; Hecox and Galambos, 1974) and associated with maturation in the CAS such as myelination, synaptogenesis, and change in fiber diameter (Salamy and McKean, 1976). These developmental processes may be responsible for the longer wave III and V latencies of the present data, but this requires histological confirmation. Whatever developmental changes occur, they appear to proceed in a tonotopic manner.

The relationship between delayed latency of waves III and V and auditory sensitivity or responsivity in infants remains obscure. All normal adult subjects showed a decrease in latency of all BSR peaks with increase in intensity up to 90 dB HL. This differs from the findings from infants (Fig. 24) where it was shown that latency of wave I to 4 kHz FCs behaves as with normal adults while for waves III and V, latencies plateau at levels of 60 dB for the youngest infant. Thus, in normal adults the L-I functions for waves I, III, and V are fairly parallel across the intensity range used, but in infants, changes in latency occurring in the cochlea (wave I) may not be reflected at more central sites. Subjects with hearing loss did not provide observable wave Is, but observations on wave V, as with normal adults, showed a consistent decrease in latency as intensity increased (the absolute latency values may have been longer than normal). Thus, the delayed latencies of waves III and V in infants cannot be simply attributed to conditions at the periphery as done with hearing loss Ss and not necessarily indicative of a "hearing deficit." However, a reduced responsivity to high frequencies cannot be ruled out either. The EMG data from infants does suggest greater responsiveness to low-frequency stimuli than to high frequencies (Hutt et al., 1968). From an ontogenetic point of view, the most important stimuli to the infant are low-frequency ones: mother's heartbeat, speech, and cooing or

humming. These stimuli are reported to sooth and comfort the infant (Bench, 1969; Birns, Blank, Bridger and Escalona, 1965) and therefore may be of evolutionary importance. High frequencies are of lesser importance in the infant's environment until late in the first year of life when the motor and neural mechanisms for speech production reach readiness. If the last segment of the cochlea to reach maturity is the apical turn, perhaps the CAS pathways associated with these apical locations are ready to conduct sometime before the cochlea can transduce the information. With this compensation, no further time would be lost once the cochlea reaches maturity, and low frequencies would be processed quite early in the developmental cycle.

A trend was observed for low (caudal) brainstem structures represented by wave III to mature before higher (rostral) ones represented by wave V. This is consistent with reports that the IC lags lower brainstem structures in degree of myelination in the newborn infant (Rorke and Riggs, 1969). The tonotopic developmental sequence was present for wave III as well as for V. Histological data confirming a tonotopic maturational sequence are unavailable.

Wave VA requires a slightly longer time to attain adult latency than wave V but this was not a consistent feature. Until the source of wave VA is determined, its importance in the developmental picture is uncertain. In clinical BSR audiometry wave VA may be quite useful in determining the presence of a response. The probability of detecting wave

VA was not much different from wave V; however, the criteria used to identify a response as present in this study was oriented toward obtaining a readable latency. With less strict criteria in a clinical situation, wave VA might be a more reliable indicator of response presence than wave V.

Threshold Determination by BSR

Data from subjects with hearing loss demonstrated that latency of wave V at elevated BSR threshold may still be within the normal latency range, or threshold latency may be longer than normal but decreases to within the normal range at suprathreshold levels. This effect has been interpreted as a physiological indicator of recruitment, a common phenomenon found in the BSR recorded from ears with cochlear hearing loss (Picton et al., 1977). One proposed mechanism responsible for recruitment in the gross VIII nerve response (rapid increase in amplitude or decrease in latency with increase in intensity) is the addition of more nerve fibers, which terminate on hair cells located in the basal turn, as stimulus intensity is raised (Ozdamar and Dallos, 1976). Since wave V reflects activity originating at the periphery, the recruitment phenomenon may be observed at brainstem levels. This physiological recruitment (via latency of wave V) was best shown by subject BJ who had a fairly flat hearing loss at 60 dB from 1 to 4 kHz. For those subjects with profound high-frequency losses recruitment of latency was incomplete to high-frequency FCs even at the highest

intensity levels. For these subjects (see Fig. 7, 1 and 4 kHz, subjects BB, JV, and EB), little or no latency recruitment was observed; the L-I functions appeared above and nearly parallel to the normal function, a characteristic usually found in subjects with pure conductive hearing loss (Picton et al., 1977). Behaviorally, recruitment is defined as a rapid increase in the sensation of loudness to small increases in stimulus intensity. A common audiological test for loudness recruitment, when a patient has a unilateral hearing loss, is the Alternate Binaural Loudness-Balance Test (ABLB) introduced by Fowler (1928). Complete loudness recruitment occurs when the loudness of a tone delivered to the ear with a loss can be matched to the loudness of the same tone in the other (normal) ear by increasing the stimulus intensity. In many patients with cochlear hearing loss, complete loudness recruitment is not demonstrated by tests such as ABLB. The relation between loudness recruitment and wave V latency is not known at this time. Future research may determine if a correlation exists.

The BSR results when used for clinical evaluation of hearing loss must be interpreted with caution. For example, if subject BJ was tested only by BSR at 4 kHz, 60 dB, and wave V latency was used as a criterion for normal hearing, she could have been diagnosed as normal. Therefore, BSR threshold value should be obtained in addition to latency of wave V at several different intensities. The BSR findings should be considered in conjunction with other tests such as

middle-ear impedance (tympanograms and stapedial reflex), behavioral responses, and the patient's history in order to provide the most accurate diagnosis.

When using the BSR for assessment of hearing in infants, the L-I function for wave V is dependent upon the age of the infant, whereas the L-I function for wave I is not age dependent (Fig. 4). If the wave V L-I function is used, a norm must be established for each age group. In using wave I, the L-I function established for adults would suffice for infants as well. Mendelson, Salamy, Lenoir, and McKean (1979) recommend that wave I be used rather than wave V for testing infants because of age-independence and good reliability. The difficulty in using only wave I is that at low intensities, wave I is difficult to record. Perhaps the best procedure for infants is to obtain L-I functions for wave I and wave V. If the wave I function is normal and the wave V function is abnormal this could be an indicator of a maturational lag in the central nervous system (CNS) and suggests that the infant should be monitored periodically.

Summary and Conclusions

1. Filtered click stimuli produce the most frequency specific responses at the lowest intensities and least specific at the highest intensities. An exact relation between PT threshold and corresponding frequency FC-evoked BSR threshold does not exist. The data suggests that when FCs are presented at 40 dB HL, the region along the cochlear

partition stimulated is approximately 1/2 octave higher than the center-frequency of the FC; at 60 dB HL the stimulated area is about one octave higher; above 70-80 dB HL all FCs stimulate the same basal location. It is questionable whether BSRs can be obtained from cochlear regions responsive to frequencies below 500 to 1000 Hz.

2. The cochlea in infants is mature at the basal turn and at least up to the region maximally responsive to approximately 1.5 kHz by one month postnatally and perhaps sooner. Little is known about the extreme apical turn.

3. The central auditory pathways are not fully mature until some time after one year of age. Brainstem pathways which carry low-frequency information appear to reach maturity by one month of age, while high-frequency pathways are still immature at one year of age. More caudal brainstem structures represented by III mature before rostral brainstem structures represented by V.

4. It is not clear what effect the delayed latencies on waves III and V have on responsivity to high-frequency stimuli in infants but data from other studies suggest that it is reduced compared to low frequencies.

5. In using the BSR for clinical, threshold determination, both threshold intensities and L-I functions should be obtained.

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BIOGRAPHICAL SKETCH

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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